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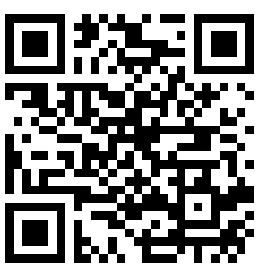

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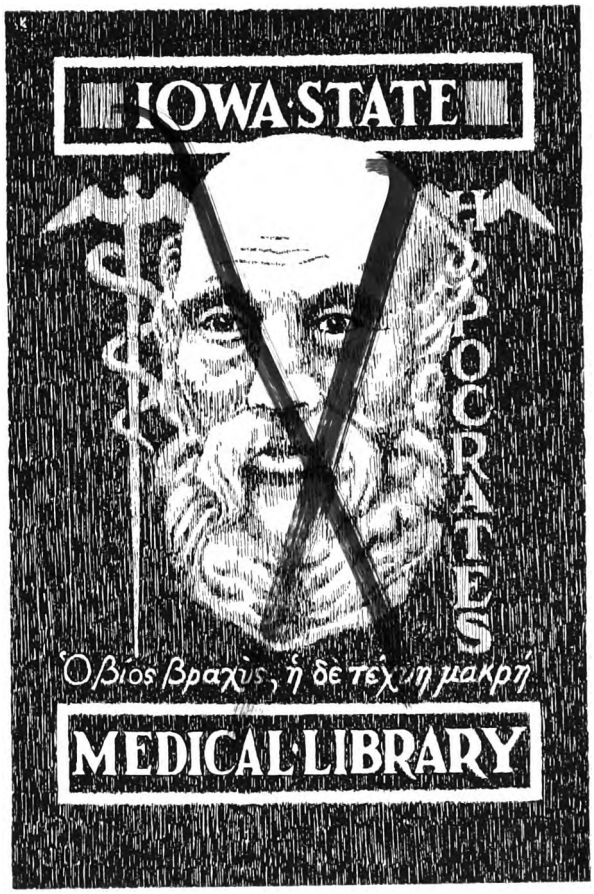

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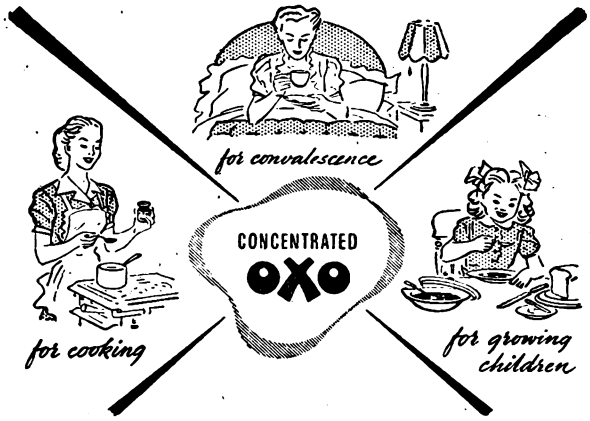

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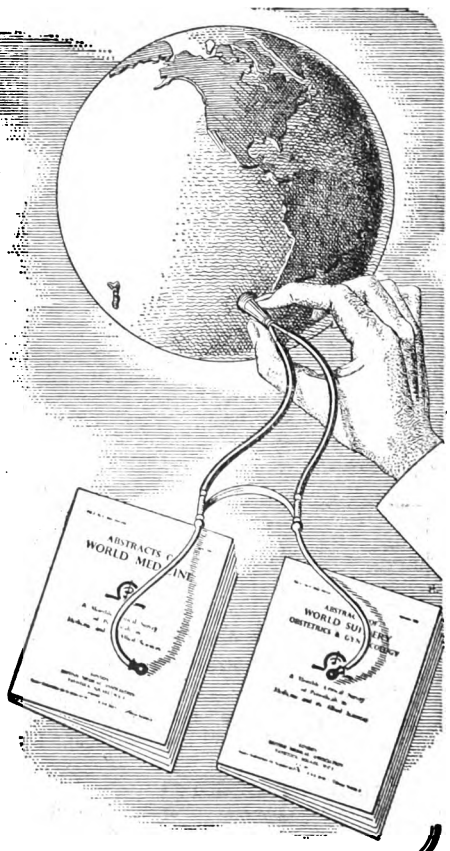

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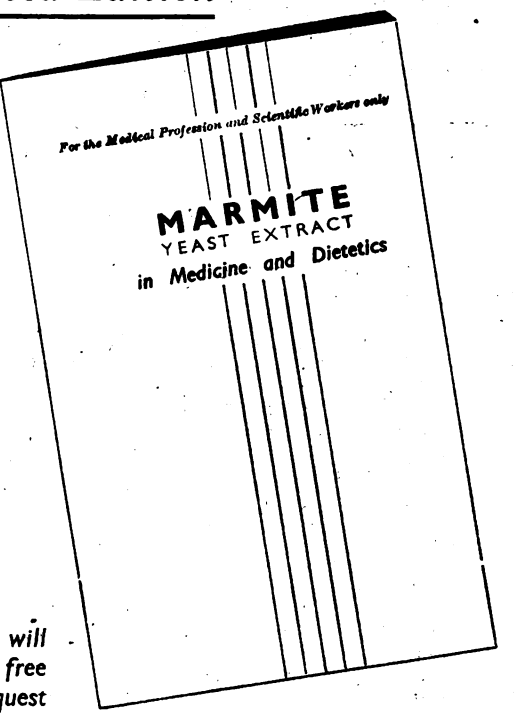

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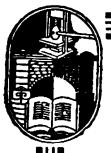

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—*Guy's Hospital Gazette.*

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CONSCIOUSNESS AND ITS DISTURBANCES

CONSIDERED FROM THE NEUROLOGICAL ASPECT *

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"Good Lord! What is man! for as simple he looks,
All in all, he's a problem must puzzle the devil."
ROBERT BURNS.

THE subject of consciousness is bound to be reviewed from time to time as new knowledge accrues, but the approach of the psychologist to it and that of the neurologist, medical or surgical, are strikingly different. The psychologist is concerned largely with introspection, with abstract ideas treated by philosophic argument, and seems perhaps to us to be under a certain subservience to words. The neurologist is concerned with abnormal appearances and failures of reactions. The psychologist starts with consciousness and proceeds to analyse it. The neurologist is apt to start with unconsciousness and, in the traditional neurological fashion, to try to make deductions about the normal from the abnormal.

William James (1893) said that everyone knew what consciousness was until he tried to define it, and no definition that has been given is completely satisfactory. I use the word to mean a sense of awareness of self and the environment, well knowing that this definition begs many questions.

Awareness of self and of the environment does not connote that the state of consciousness has two parts, one of self and one of the environment, for the environment is obviously in relation to self and inseparable from it. Awareness of self, however, requires a little further consideration. It is not merely that I am aware of myself as a person whose presence and activities are visible to the outside world, but also I have a feeling that "I" am aware, that I know that I am, and that I see and feel and act. This feeling ("I, the knower") constitutes "the very self," as Hughlings Jackson (1925) put it.

Without going into any philosophical subtleties it is not difficult to see where the psychologist's difficulty in definition lies. "Know" is a transitive verb, and I cannot know (or be aware) without knowing (or being aware of) something—there must be a subject (I the knower) and an object:

I	know / or / am aware of	my bodily self / my environment / certain qualities in my mental self

We can elaborate the objective side of this scheme. It is the subjective side, "I, the knower," that is so elusive, because anything I know about him will go to the objective side of the scheme. Kant taught that it (subjective consciousness) "does not reveal itself but only its objects. So far as our mental states are known at all, they are known objectively as we know outside bodies . . . they are objects of consciousness." We, as practical people, cannot help thinking that this sharp distinction between subjective and objective is partly a matter of language and syntax, and that it should be possible to find a formula which avoids the apparent antithesis. William James attempted to find such a formula; and, though the subject is age-old and obviously fundamental for psychology, a simplified conception of consciousness merely as a state of awareness dates only from his time. For William James subjective consciousness became merely "the stream of thought" or "thought goes on." Subjective consciousness "is the name of a nonentity and has no right to a place among first principles." Bertrand Russell (1946) says that on this ground alone James deserves a high place among philosophers. To regard consciousness as a *state* of awareness is certainly serviceable in medicine but we must not entirely overlook the subject-object relationship implied in the word "awareness."

The neurologist's approach is objective, and strictly we cannot know that another being has an awareness of himself and his environment; but as practical men and physicians we know that all men are formed on the same pattern, and their behaviour and conversation confirm our belief that they have the same feelings of awareness as ourselves, and in studying them we can study consciousness. In general we can be confident that the subjective and objective approaches bring us into the same territory, but at the margins our fields do not quite correspond. In some directions the neurologist is apt to apply the word "consciousness" too widely. Contrasting it with unconsciousness, which usually denotes a state below sleep, a state of unreactiveness, we sometimes use "consciousness" to denote merely a state of wakefulness. A baby a few weeks old has probably no awareness of self; yet the words "conscious" and "unconscious" are used in regard to it, and even in regard to young animals, such as puppies. This wakefulness is very close to William James's "thought goes on." But there are states of automatism and post-traumatic excitement which are also states of wakefulness with deficient, if any, awareness; yet we do not say that the patient in automatism is "conscious." Hence we are not consistent in our use of the word. The inconsistency, however, is verbal—i.e., at the boundaries our usage does not exactly conform to the dictionary meaning of the word. These margins of the field of consciousness are in general not accessible to the psychologist, though Freud's methods, hypnotism, and other techniques enable him now to range nearer to them than formerly.

As neurologists we are concerned with the states in which we find our patients: whether or not they seem to have that awareness of themselves and the environment which the normal person seems to have, and if not, how they differ from the normal. We are concerned with the ways in which they become unconscious, and with the lesions, especially the sites of the lesions, which seem to be responsible for the loss or disturbance of consciousness. When consciousness is disturbed the analysis of symptoms is difficult, and various states and phenomena still await elucidation; but in the last twenty-five years we have learnt to recognise certain disturbances of a kind previously unsuspected, to which I must make reference.

States of Consciousness

Allowing for marginal overlap we can divide the states of consciousness in which we observe our patients into four groups: (1) the normal condition, in which the person is responsive and reacts to psychological stimuli and indicates by his behaviour and conversation that he has the same awareness of himself and his environment as ourselves; (2) sleep, a condition of inactivity from which he can be roused and resumes his normal state; (3) a state of unconsciousness in which he appears to be deeply asleep but cannot be roused to normal consciousness; and (4) a much less common state, or group of states, in which the patient is awake and active but gives evidence that he is not completely, if at all, aware of himself and his doings, and of which he has no recollection afterwards; such are the states presented by certain epileptic equivalents, postepileptic automatism, and post-traumatic excitement; probably delirium belongs also to this group.

* The Lumleian lectures for 1947 delivered at the Royal College of Physicians of London on April 16 and 17, 1947 (slightly abbreviated).

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NORMAL CONSCIOUSNESS

The normal state may fluctuate in the course of the day within a wide range, from intense attentiveness to drowsiness or to deep abstraction of thought with greatly reduced awareness of self and of much of the environment. It must vary from one person to another, for the stolid and stupid person cannot have the same average degree of awareness as the alert, intelligent, and cultured person who is aware of so many more things with such greater intensity. It may vary also with the mental "depth" of the individual. We may admit also a hypernormal state, a manic awareness of every detail of the environment.

SLEEP

Sleep is a buffer state between consciousness and unconsciousness; it is a state of unconsciousness into which the messengers of consciousness can penetrate. It is bounded on the hither side by a belt of broken country which Sir Thomas Browne called "the drowsy approaches of sleep," and beyond that it extends just as far as consciousness can exert its influence. Beyond that curtain is unconsciousness. A person in sleep, if not disturbed, gives little evidence of being aware of himself and his environment. Theory postulates that some kind of barrier is erected which impedes the passage of the impulses roused by the numerous stimuli from the environment and prevents them from reaching his higher cerebral centres. But the gate is easily crashed, and if he is not deep in sleep he can be quickly recalled to consciousness by a slightly unusual stimulus, such as a shake or a noise. If he is deep in sleep, away towards the boundary of unconsciousness, he is much less responsive to the call of consciousness. Moreover the gate-keeper is conditioned, or perhaps the higher centres are conditioned, so that an accustomed stimulus, though of considerable intensity, will not recall the sleeper to consciousness, but a lesser unaccustomed one may do so, or the cry of the child with its appeal to emotion, may bring back the mother from sleep when many louder noises are neglected. It is this subordination to consciousness, this liability of the sleeper to be recalled at a moment's notice to consciousness, that distinguishes and demarcates sleep from unconsciousness.

Delicate and elegant confirmation of some of these effects has been given by the electro-encephalograph, which records the periodic changes of potential, or discharges from cell groups, of the cerebral cortex. When afferent impulses of one of the sensory receiving areas of the brain are minimised—e.g., in the visual areas when the eyes are closed—the changes of potential in that cortical area become synchronous, and a much stronger and more rhythmical record is obtained—the so-called alpha rhythm—having a frequency of about 10 per sec. Records similar to those obtained with pad electrodes placed on the scalp can be obtained with needle electrodes placed directly on the cortex of the brain, and there is little doubt that they are those of an electrical element of the metabolism of cortical cells in activity. Now the records obtained from people asleep differ much from those from the same people awake. The records from people who are deeply anæsthetised, or are in coma from any other cause, are different again. Accounts of these were published by Davis et al. (1938) and Loomis et al. (1938) and have been amply confirmed since. When a person with electrodes fastened on his scalp becomes very drowsy, the alpha rhythm becomes less regular; and, as light sleep comes on, it becomes interrupted here and there where waves have fallen out. As sleep deepens, the alpha rhythm ceases and waves of a frequency of about 6 per sec. appear; in very deep sleep these disappear in turn and long slow waves at the rate of 2 per sec. are seen. In deep narcosis even these cease and little or no electrical activity can be detected.

To revert, however, to natural sleep, Loomis et al. (1938) showed by electro-encephalography that the sleeper is sensitive to stimuli from his environment and even though he may not waken he nevertheless discriminates between different kinds of stimuli. In a particular instance traffic noises outside the house had no effect on the electro-encephalogram of a sleeping person, but a slight noise in or near his room—the snap of an electric-light switch—would change the record towards the waking type. If after such a stimulus the sleeper does not waken, the sleeping type of rhythm is resumed; but, if he wakens, the normal rapid alpha rhythm is instantly restored.

Dreaming is another alteration within the sleeping state, and the occurrence of dreams in response to touch and other stimuli is further evidence that the sleeper is not completely insensitive to this environment, even though the stimuli may be misinterpreted or perhaps deliberately given an altered significance. Moreover dreams leave their own impression in memory which may afterwards be recalled, but in the state of unconsciousness no impression, so far as we know, is left.

COMA

Ordinarily in disease unconsciousness is entered by way of sleep, and emergence is by the same route. With epilepsy and trauma the entrance is otherwise, but the emergence usually appears to be through sleep. For the artificial unconsciousness of anæsthesia also entrance and return are through sleep.

The outstanding fact about the unconscious patient is that he cannot be roused to consciousness. If he is not far beyond the curtain he responds in various ways to physical stimuli; he moves or grunts and perhaps even raises his hand to rub a part pricked; in certain instances he may be very resistant and irritable; but he cannot be recalled to consciousness. If he responds to small stimuli by grimaces or other movements, it may seem that strong stimuli would recall him to consciousness, but they do not do so. Though sensitive to physical stimuli he remains obstinately unconscious; he gives no evidence subsequently that his mind was aware of the disturbance. To psychological stimuli he usually shows no response, but in some instances he may be roused to utter his name in answer to a loud question; but he answers like a man asleep and has no recollection of it afterwards. As in deep sleep, the plantar reflexes are extensor, showing a deficiency of activity in the controlling motor centres.

The electro-encephalogram of coma has already been referred to. If coma deepens and the patient passes towards death, the electrical activity becomes less and less. In some conditions of unconsciousness where the patient is irritable and mobile the record reveals much irregular electrical activity in the cerebral cortex, but it seems likely that these cases belong more truly to the next group.

UNCONSCIOUSNESS OF EPILEPSY, &C.

There is another unconsciousness which has nothing to do with sleep. In Jacksonian epilepsy the attack begins with a local convulsion, the outward manifestation of abnormal discharge in a restricted area of cerebral cortex. As the convulsion spreads, the patient becomes unconscious; usually he becomes unconscious by the time the convulsion involves the whole of one half of the body, and certainly by the time it shows any extension to the other half. Unconsciousness is reached through convulsion, or perhaps we may say through phenomena of abnormal cortical discharge—i.e., by way of an irregularity or perversion of cortical function. In the major epileptic fit unconsciousness is associated with the same kind of disturbance (though it is possible that this is not primary), and in petit mal we have every

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reason to believe that the unconsciousness has essentially the same basis. There is a whole group of conditions of the nature of automatism in which we suppose the highest cerebral functions are temporarily abolished as the result of a similar process, and in some of these, though memory is temporarily abrogated, the disturbance of consciousness may be partial—the patient's conduct may reveal that he is not completely unaware of himself and his environment.

One of my patients during his period of automatism, for which he had complete amnesia, invariably complained of a pain at the back of his head (from which he also suffered at other times), thus showing that he had an awareness of his body, and his behaviour displayed considerable awareness of his environment too.

Also belonging obviously to this group are partial disturbances of consciousness associated with those incidents which we call sensory fits—incidents in which hallucinations of sight or hearing, taste, smell, or common sensation are provoked by discharges in the corresponding sensory systems. Finally, in some of the conditions of post-traumatic automatism and post-traumatic excitement it is evident that the disturbances of consciousness have no relation to sleep, and while it would be going too far to assert that they have an exactly similar basis to the conditions I have been referring to, that is, at least, a reasonable surmise.

Consciousness and the Electro-encephalogram

The electro-encephalograph records periodic changes in the electric potential of cerebral cells, and it seems that these must represent a periodicity in their metabolism. Similar records can be obtained with needle electrodes placed directly on the cortex, and there is no doubt that they arise from the cortex itself. Moreover, Dusser de Barrenne and McCulloch (1941) found that the three layers of cortex external to the layer of large pyramidal cells could be removed by thermocoagulation without any considerable effect on the electrocorticogram; hence the rhythm is due to, or at any rate dominated by, the three deeper layers.

In referring to sleep I mentioned that the alpha rhythm could be obtained from the occipital cortex of a patient in a normal state of wakefulness, whereas in deep sleep and coma it was abolished and replaced by long slow waves, and, in general, the normal state of wakefulness is characterised by fast rhythms. It would, however, be premature to conclude that consciousness and fast rhythms are inevitably associated. Indeed this is not so. Under certain anæsthetics, especially in light ether anæsthesia, fast rhythm persists while the patient is unconscious, and the same obtains in animals under light anæsthesia with various barbiturates. It is this last fact which has made possible much of the experimental work on the electrocorticogram. We can, however, say that, in the absence of anæsthetics and certain drugs, there is a close association between the alpha rhythm and normal wakefulness.

While the unconsciousness that is beyond sleep is associated with the depressed cortical activity indicated by long slow waves at 2 per sec., the unconsciousness related to epileptic phenomena is usually associated with excessive and irregular electrical cortical activity —e.g., during an epileptic fit or petit mal. We may perhaps put alongside this the unconsciousness in the excited stage of ether anæsthesia. If an electrical record could be obtained in a patient unconscious in a state of post-traumatic excitement, probably exaggerated rapid potential changes would also be disclosed. The two different kinds of departure from the normal electro-encephalogram with which unconsciousness is associated are both seen in relation to an epileptic fit, because the unconsciousness at the onset is usually accompanied by excessive and irregular cortical electric changes, but the continuing unconsciousness after the fit is associated with an extinction or profound depression of electrical rhythms.

I may refer at this stage to another observation of electro-encephalography which is of the greatest importance for our subject. It was found by Lewy and Gammon (1938) that, when fibres passing between the thalamus and the cortex of a cat were experimentally divided in the internal capsule the electric activity of the corresponding area of cortex was practically abolished. This phenomenon was subsequently studied in greater detail by Dusser de Barrenne and McCulloch (1941), who found in experiments on animals that the rhythmic electrical changes of any area of sensory cortex were at once abolished if it was undercut so as to divide its connexions with the thalamus and its other descending fibres. So long as these were intact, the portion of cortex might be isolated (by making encircling cuts round the area) without interfering with its electrical activity, and destruction of all the rest of the cortex made no difference to the electrocorticogram of the selected area. Whether this obtains also in the human brain, where the association tracts are so much more important, has not yet to my knowledge been determined, but from other evidence we know that the dependence of the cortex on the thalamus is so great that it probably does obtain.

In a recent case at the National Hospital in which a patient had a tumour in his right thalamus, with severe loss of postural sensation on the left half of the body, the electro-encephalogram from the right parietal lobes consisted of the long slow waves characteristic of sleep and indicating greatly depressed activity.

Division of corticothalamic connexions has a similar effect on the sensory nucleus of the thalamus, the electrical activity of its corresponding portion being greatly and permanently diminished.

The whole significance of these findings is not yet clear. Perhaps depression of the activity of cells, consequent upon division of their axons, largely explains it, but it is clear that intervention between the thalamus and the cortex to all intents abolishes the activity of the cortical area concerned.

"The Seat of Consciousness"

Is there any part of the brain with whose activity consciousness is particularly associated? In the time of Galen consciousness dwelt in the lateral ventricles; when these Lumleian lectures were instituted, its home was in the pineal body or in the corpus striatum; since the time of Hughlings Jackson and Ferrier it has generally been accepted that consciousness depends on activity of the cerebral cortex, but to some the evidence has not been perfectly convincing. Jefferson (1942) has lately expressed his belief that consciousness ("except in the widest psychological connotation") has very little to do with superficial grey matter; that it is a primary function located in the more ancient parts of the brain—in the hypothalamus, possibly in the basal ganglia and in the brain stem. In my experience there are three sites where local lesions cause severe disturbance of consciousness as an outstanding symptom: (1) the hypothalamus; (2) the upper half of the brain stem; and (3) the cerebral cortex.

THE HYPOTHALAMUS

Since Cushing first described pathological sleep as one of the symptoms of pituitary tumours it has been known that lesions in this area may give rise to profound disturbances of consciousness, and many instances have been recorded. Jefferson (1944) has described a case in which the cause of unconsciousness and death seemed to be merely a clot of blood filling the hypothalamus. There is also much experimental work which indicates that this area exercises a control over sleep and waking.

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The sleep that occurs in the clinical cases is to outward appearances the same as normal sleep, but it is liable to pass into coma and on into death. Many such cases have been recorded.

Walter et al. (1939) described a case of a tumour of the hypothalamus with prolonged coma in which they studied the electro-encephalographic features. They found that the electrical potential changes were uniform over all parts of the head and were everywhere the slow (2 per sec.) waves characteristic of deep natural sleep. The more rapid rhythms had everywhere disappeared, and there was no suggestion of any local variations of the electrical activity over the hemispheres.

Obrador Alcalde (1943) has found experimentally that a lesion at the base of the hypothalamus in an animal under 'Nembutal' anæsthesia at once abolishes the spontaneous electrical activity over the whole cerebral cortex.

Are we to conclude that here is the seat of consciousness—here is surely the hiding place of the elusive ego? Let us consider the matter a little further. Both in the clinical and in the experimental case we have a general effect—uniform over the whole cortex—produced by a local lesion. Almost all that we know otherwise of the hypothalamus is that it has a control over vegetative functions—water metabolism, sugar metabolism, heat regulation, and the like. If water metabolism is disturbed by a lesion of the hypothalamus, are we to say that the hypothalamus is the seat of water metabolism? We know that it is not. Is it the site of heating and cooling? Of course not.

By analogy is it not most likely that the influence of the hypothalamus on the electrical and other activity of the cerebral cortex is also vegetative—i.e., to maintain the metabolism of the cells and see that energy is provided for cortical activity? There is considerable evidence that the hypothalamus has such a function. If so, the effect of lesions of this portion of the brain on consciousness may be a consequence of their effect on the activity of the cerebral cortex, and we would be no more justified in describing it as the seat of consciousness than as the seat of water metabolism. At any rate let us take note of the fact that it has this influence on the cerebral cortex.

THE BRAIN STEM

If we study a series of cases with progressive lesions in the lower parts of the central nervous system, we find that as long as the lesion is in the spinal cord or the lower half of the brain stem the consequent signs and symptoms are those which result from the disturbances of function of the local structures and the long tracts—assuming that shock is not an important factor. But when the lesion is as high as the middle of the pons an effect of a more general and entirely different order may appear in that the patient becomes first drowsy, then unrousable and passes on through deepening coma to death.

Some years ago I had under my care at the National Hospital a woman of 56 who was admitted with a disturbance of sensation down the left side of her body, a weakness of the right side of her face, and a loss of the lateral movements of her eyes. These last two signs accurately indicated the level of her lesion at the middle of the pons, and her loss of sensation showed that it had affected the median fillet on the right side.

The manner of onset of her symptoms suggested that she had a slow cerebral hæmorrhage, and in the next ten days the lesion evidently spread to involve the median fillet on the other side, because she then lost sensation on the whole of the right side also. She had been drowsy from the time she came in; but, when both sides had become anæsthetic, it became impossible to keep her awake. She had become deaf too, and so, when she closed her eyes, all her channels of reception of impressions from without were interrupted, except her sense of smell, and I am afraid it did not occur to us to make much use of that.

In these circumstances she fell into a deep sleep; and, even when we raised her eyelids, she did not rouse properly, and in the course of a few days of gradually deepening coma she died. After death the diagnosis was fully confirmed. She had, at the level of the middle of the pons, a hæmorrhage, which had spread horizontally to involve the whole of the median fillet on each side and the adjacent lateral fillets, and other auditory structures, as well as the 6th nuclei and the right facial nerve. All the anterior part of the pons, including the pyramidal bundles, was intact.

Now why did this patient pass into coma? No structure that is individually vital, so far as we know, was involved. Much the most important structures affected were the median fillets, and because of the interruption of both of them at this level the patient must have been completely deprived of awareness of her body. She had lost hearing, but vision was left to her to maintain contact with the outside world; nevertheless, we found it impossible even by keeping her eyes open to bring her back to consciousness, and I have had the same experience with other similar cases. Can it be that an awareness of the body is essential for consciousness?

There is a site here in the upper pons and mid-brain at which a relatively small lesion may interrupt all the afferent tracts except the visual and olfactory pathways. At a lower level hearing will be left intact, and slightly lower still sensation from the important face and mouth areas will persist.

Various experimental findings confirm the view taken of this case. Bremer (1936, 1937) found that, after division of the brain stem at the mid-brain level, animals passed into coma, with electro-encephalograms typical of very deep sleep. When the transection was below the pons, leaving the auditory nerves intact, the sleep was less deep, the animals occasionally roused slightly, and at such times rapid rhythms were recorded in the electro-encephalograms. Moreover, when an animal thus operated on was "asleep," noises would cause changes in the electro-encephalogram, with the appearance of fast rhythms not only in the temporal auditory areas but also to some extent over other parts of the brain. (This is not to say that the animal was conscious of the noise.) Lewy and Gammon (1938) also found that the electrical activity of the cortex of the cat under nembutal anæsthesia was abolished by section of the mid-brain, and they deduced that the spontaneous rhythm in the cortex depended on intact sensory pathways. They also found in other animals that, when the electrical activity of the cortex was abolished by deeper anæsthesia, stimulation of the sensory tracts in the brain stem would arouse bursts of rhythmical activity in the cortex lasting some minutes and resembling normal activity.

The evidence is strong that, if nearly all the sensory pathways are interrupted, the activity of the cortex is greatly depressed or abolished, and we may have to infer that it is for this reason that a lesion in the pons or in the mid-brain may cause unconsciousness, because we do not know of any structure in this region that presides in any more specific way over consciousness.

THE CEREBRAL CORTEX

Negative or paralysing lesions in the cortex must be very extensive to cause unconsciousness, and many are not of much value for our argument because they may produce indirect effects on other parts of the brain also. Many lesions in the cerebral hemispheres may disturb cortical function extensively by interfering with thalamo-cortical connexions; but often in such cases there are confusing factors such as raised intracranial pressure and shock which may have their own effects on consciousness.

So far as paralysing lesions go, some of the relatively serviceable cases for our purpose are to be found among the cases of subdural hæmatoma. The hæmatoma is a membranous envelope containing altered blood which overlies the cortex and gradually enlarges. It does not

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directly involve any cerebral structure, and in most instances it does not cause any considerable rise of intracranial pressure. These hæmatomas become very extensive and are often bilateral, and in nearly all cases drowsiness is an outstanding symptom and periods of coma are common. Such symptoms may develop when no abnormal motor phenomena can be detected.

A man had severe headaches for several months and during that time had become gradually less active and liable to periods of drowsiness. Then he began to sleep for considerable parts of the day, and there were times when his wife was unable to rouse him. He was usually at his best during the afternoon and was then free from headache and mentally clear. Later, when he was under observation in a nursing-home, he remained in a stuporose condition most of the time, but still answers could usually be obtained from him. Finally he remained unconscious a whole day and died that evening. Post mortem a moderately large subdural hæmatoma over the convexity of the right cerebral hemisphere and a small one on the left side were found.

The symptoms in such cases seem to be attributable to the direct effect of the pressure of the hæmatoma on an extensive area of cortex, because if this is removed their relief is immediate. I have twice had the experience of seeing a patient, taken stuporose into the theatre, wake up on the operating-table as the contents of the hæmatoma flowed out through a burr hole. However, even these cases are not free from objection by those who believe that the seat of consciousness is at a lower level.

Better evidence of the effect of disturbances of the cortex on consciousness is provided by lesions of the irritative or discharging type. The argument that Hughlings Jackson brought forward depended on the association between disturbance of consciousness and fits which, as he had shown, were consequent on cortical lesions. Loss of consciousness might occur in a fit either before the spreading excitation reached the motor areas or after the motor area had been for some seconds or more in a state of abnormal discharge. A typical passage is as follows:

"To lose consciousness is to lose the use of the most special of all nervous processes whatsoever. Now, one of the many ways in which the use of them may be lost is by their being the seat of an epileptic discharge. It will be temporarily lost during every discharge . . . just as the use of an arm is lost during the severe spasm of its muscles. . . . If the discharge be slight there may be, as appears, loss of consciousness only. This is so in very slight cases of petit mal. If it be strong the discharge spreads from these very highest centres to lower centres . . . with which they are, therefore continuous; . . . there is loss of consciousness followed by convulsion."

The loss of consciousness continuing after the fit he attributed to exhaustion of cortical centres by discharge.

These ideas of Jackson's have all been confirmed in a remarkable way by the electro-encephalograph; it reveals not only widespread cortical discharge at the time of a fit but also widespread momentary discharges associated with the transitory unconsciousness of petit mal. After a fit there is a period of extinction of the cortical electrical activity, which may last fifteen or twenty minutes.

These observations indicate that in epileptic conditions associated with unconsciousness there is disturbance of the cortex over a wide area, but Jackson's evidence from local discharging lesions was perhaps more important. If abnormal discharges are localised to an area having a sensory function and relatively isolated—e.g., in one temporal lobe—the patient experiences a hallucination but does not altogether lose his "normal" consciousness. In a case of temporal-lobe fits the patient has usually a formed visual hallucination accompanied or preceded by a sensation of taste or smell—i.e., instead of seeing merely flashes or balls of fire, as he may with occipital discharges, he sees formed objects, often people, or a whole scene. One of my patients said that in the attack "my mind seemed to move sideways." By this I think he meant that he suddenly seemed to see a new environment though he knew that his body had not moved—i.e., he was still partly aware of the "old" environment. In other words he had a kind of double consciousness—one part true and the other false—or, as Hughlings Jackson put it, "a mental diplopia." The patient's wife said that at the time of such a turn he seemed "vacant," and we know that in such cases there is an impairment of general consciousness, an impairment of the awareness of self and the environment. Jackson recognised these disturbances as focal fits, and he had shown that the lesions with which such attacks were associated involved the cerebral cortex.

Judging them from the evidence of cases of different kinds of organic lesions the relation of cortical disturbance to consciousness seems to be such that: (1) a lesion causing widespread depression of cortical function is associated with unconsciousness or drowsiness; (2) widespread interference with cortical activity by irregular discharges is associated with unconsciousness; and (3) focal disturbance of cortical activity by localised irregular discharges is associated with partial disturbance of consciousness.

The scheme which we see developing seems to show consciousness depending on some activity of the cerebral cortex, an activity more or less parallel to, but we cannot say identical with, that which produces the alpha rhythm—an activity which lapses when the function of the hypothalamus is seriously impaired, and which lapses also if the sensory tracts in the upper half of the brain stem are interrupted. We have not seen any indication that there is any localised area or focus with which it is peculiarly associated. In fact the weight of evidence is undoubtedly the other way, and suggests that the whole cortex shares in this particular activity. It must not be supposed that, because an area of cortex is regarded as being primarily concerned with some sensory or even motor function, it is any the less concerned with consciousness.

But our surgeons now remove large areas of cortex and say that they observe little change in consciousness. Jefferson (1942) reported on 118 cases of lobectomy performed by himself alone, and his total is doubtless considerably higher by now. About 60% of these were removals of one or other frontal lobe, and one of the earliest was a case of mine. Also, the operation of leucotomy, which is in full fashion, consists in the division of the frontal thalamocortical connexions on both sides, and must have the effect of abolishing or greatly reducing the activity of extensive areas of frontal cortex.

The surgeons, and in fact all of us, are impressed by the slightness of the ill effects resulting from these procedures. That is not to say, however, that there are no mental symptoms and no change in consciousness, and certainly the persistence of consciousness after removal of a portion of the cortex (in no case more than a tenth) does not justify the argument that consciousness has very little to do with the superficial grey matter.

It is obviously important that we should learn from the more pronounced cases to identify the lesser changes that occur in others, so let us see what they are.

I mentioned earlier the quality of "depth" of mind—an imprecise term perhaps, but one which is capable of very fair definition, as we recall from Hazlitt's (1826) essay on the subject. There are depth of thought and depth of feeling; and, while we are concerned here with the former any alteration always seems to involve the latter as well. Depth is that quality by virtue of which a psychological stimulus arouses a large number of associations in the mind, many of them of an abstract or general character, and it must depend on richness of

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neuronal connexions. Depth is often associated with a certain slowness, and superficiality with an undue quickness of response.

Now I should say that the most constant and evident change resulting from frontal lobectomy or from leucotomy was an impairment of this quality of "depth" of mind or thought. But this is accompanied, especially in the psychiatric cases, by a pronounced diminution of the consciousness of self, and a relief of obsessional preoccupations and of morbid depression.

It seems to me that this loss of depth of mind and diminution of the consciousness of self are not unrelated. The order of the objects of consciousness is bodily self first, environment next, and abstract matters third—or, as William James (1893) put it, "its own body first, its friends next, and finally its spiritual dispositions must be the essential preoccupations of every human mind." All will agree that in cases where the syndrome of frontal-lobe defect is pronounced the "spiritual dispositions" and abstract thinking suffer severely and consideration for friends is greatly reduced. When to these is added diminution of the awareness of self, we have a reduction of consciousness over its whole field. Reduction of the consciousness of self may be the most evident, especially when the self has occupied consciousness unduly, but it is by no means the only effect.

Temporal lobes too are sometimes removed. I do not know what mental changes, if any, are observed after the operation, but in view of the well-known effects (dreamy states) produced by abnormal activity in the temporal cortex it will hardly be claimed that this area is devoid of influence on consciousness.

(To be concluded)

HIRSCHSPRUNG'S DISEASE AND IDIOPATHIC MEGACOLON

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BY "megacolon" we mean segmental or total dilatation of the large intestine. We are not concerned with symptomatic megacolon, in which an organic cause is demonstrable. This paper deals with the condition hitherto called idiopathic megacolon.

From a review of 73 cases of idiopathic megacolon, which have been under the care of the Hospital for Sick Children in recent years, we offer evidence which re-establishes the original conception of Hirschsprung's disease as a separate entity. Two main groups have emerged from this analysis.

GROUP I: HIRSCHSPRUNG'S DISEASE

Clinical Picture

Group I comprised 39 children, of whom 36 were boys. They were aged from fifteen days to fifteen years and presented the familiar picture of Hirschsprung's disease (Hirschsprung 1887). All the children except those who have died have been examined by F. D. S.

The history begins at birth, or very soon after, with constipation. The passage of the first meconium stool is usually delayed for several days (92 ± 3% of normal infants pass meconium within the first twenty-four hours). The severity of constipation varies from one small motion a day to inability to evacuate spontaneously for weeks. Gaseous abdominal distension usually develops within the first few months; it may be of insidious onset, causing little if any concern, or it may appear suddenly, preceded or accompanied by vomiting, and presenting the dramatic picture of acute intestinal obstruction in the newborn. These attacks may subside spontaneously, with release of flatus and immediate recovery, but in severe cases passage of a flatus tube, colon washouts, or even laparotomy may be necessary.

The survivors of these precarious early days develop chronic abdominal enlargement, and acute attacks of distension and obstruction may become superimposed. Vomiting again accompanies these acute obstructive attacks.

There is rarely any abdominal pain. Active peristaltic efforts of the bowel are audible as loud resounding borborygmi, and large quantities of foul flatus are passed per rectum.

The stools are characteristically very small rabitty pellets when hard, or thin toothpaste-like ribbons when soft. Fluid fæces are ejected at times with great force. Defæcation is painless and is accompanied by much ineffectual straining, but there is no fæcal incontinence.

Examination in the early weeks of life reveals the classical picture of acute intestinal obstruction in the newborn, with the tense rounded shiny tympanitic abdomen. Later, permanent abdominal enlargement develops, with seething peristaltic waves and palpable fæcoliths partially masked by the overlying cushion of gas. The distension is greatest in the upper abdomen; the ribs become flared, the diaphragm raised, and the umbilicus everted and apparently situated lower on the abdominal wall. Rectal examination reveals a clean anus, a normal sphincter, a well-formed anal canal, a small empty or nearly empty rectum, and perhaps spasm in the region of the upper rectum. The loaded sigmoid colon may be palpable through the rectal wall.

Besides the general clinical pattern just described there were in some cases other features which appear to us to be of some importance.

In 4 cases there was an *anal membrane* which was perforated digitally soon after birth. These cases cannot be interpreted as instances of organic obstruction, since their subsequent course conformed to the general pattern of Hirschsprung's disease.

A moderate *anæmia* has developed in 4 cases. In 2 other children the amount of hæmoglobin dropped to 35% and occult blood was present in the fæces.

Usually the impacted fæcal masses, when removed by bowel washouts, seemed old, rather dry, and not unduly offensive, but occasionally we observed an extraordinary degree of *putrefaction* on evacuation of the intestinal contents, and sometimes this seemed to have led to diarrhœa, dehydration, and vomiting.

Attacks of *acute intestinal obstruction* developed in 18 cases in the first month of life, and in 8 other cases between the first and sixth months. Only 3 in the neonatal group died during the attack; the remaining 23 survived with conservative treatment consisting of passage of flatus tube and bowel washouts.

Results of Treatment

Many forms of treatment were adopted. General medical measures included abdominal massage, binders, tipping of the bed, and dilatation, various purgatives, and parasympathomimetic drugs; but none brought permanent alleviation.

Of 25 children who received one to seven spinal anæsthetics, some showed a transient improvement, but 19 remained uncured and 6 died. Presumably because of these unpromising results, only 3 of this group had sympathectomy operations. Improvement was apparent in 2 of them, but it was temporary.

No improvement was obtained in 2 cases with colopexy. Total colectomy was performed in 2 cases and partial colectomy in 3: 1 child died a few days after total colectomy, and in 3 others the symptoms recurred, with

* Working with a grant from the Nuffield Foundation.

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dilatation and hypertrophy of the bowel proximal to the anastomosis. In 1 case, treated by Paul-Miculicz sigmoidectomy, closure of the colostomy has proved impossible on four occasions.

Colostomy was performed in 8 cases, in 2 of which it was a life-saving emergency measure. All the children improved considerably after colostomy, but 1 died two months later from gastro-enteritis which was epidemic in the ward. In the other 7 cases symptoms returned after closure of the colostomy. In 3 cases several attempts at closure were necessary.

We have been struck by the high mortality in the series reported by Zuelzer and Wilson (1948), in most of which laparotomy was performed. Of the 3 neonatal deaths in our series 1 followed laparotomy.

In 36 of the present cases the disease proceeded to the chronic stage, running a precarious course of chronic intestinal obstruction with superadded recurrent attacks of acute obstruction. Of these 36 children 8 died; so the total number of deaths in this group of 39 cases is already 11. The causes of death in the 8 chronic cases were as follows: 3 children died suddenly for no apparent reason; 2 died from unrelated causes (tuberculous meningitis and gastro-enteritis); 1 died of postoperative peritonitis; and concerning 2 cases no information is available.

All 28 survivors in this group were in urgent need of treatment at the start of the survey. This shows that no form of treatment hitherto described has cured the condition.

GROUP II: (IDIOPATHIC MEGACOLON)

Group II comprised 34 children, of whom 25 were boys. Their ages ranged from 18 months to 21 years. They presented a clinical pattern differing in many respects from Hirschsprung's disease.

Clinical Picture

Constipation is often present in mild form from birth, but is usually overcome by mild aperients. There is no evidence of delay in the passage of meconium. Several months or years later a more severe type of constipation develops. Abdominal distension arises less frequently and usually later than in group I, and fæcal masses, as opposed to gaseous accumulations, are more apparent. Vomiting is infrequent. Intestinal colic is common and often precipitated by purgatives which are so freely administered. Borborygmi and flatus are less apparent in this group. The fæces are of large diameter, often hard, and streaked with blood. Defæcation is accompanied by much straining and sometimes pain. This sequence of events leads the child to hold back motions, and accumulated fæcal masses distend the rectum. Soft and newly formed fæces are massaged past this fæcal plug, causing a paradoxical diarrhœa or an overflow incontinence.

Examination of the abdomen reveals many fæcal masses and less often gaseous distension. The circumanal region is soiled with fæces, the sphincter is normal, the anal canal short, the rectum full to capacity with fæces, and the rectal walls are flattened against the walls of the bony pelvis.

Results of Treatment

Children in this group are relatively fit, and the condition seems to run a benign course, responding to medical measures, with relapses from time to time. A considerable number have been cured by repeated regular bowel washouts over several weeks or months.

Of the 34 children 8 had had some form of operation on the sympathetic nervous system. The results were interpreted as successes, but in view of the fact that they would all have had thorough bowel preparation before operation we are uncertain of the part the operation played in alleviating the symptoms.

Some of these children presented with multiple fissures of the anus, piles, and prolapse as a result of constipation and straining. These minor sequelæ responded quickly to relief of the underlying condition. Some children in this group displayed features which might be interpreted as psychogenic. As a result of pain on defæcation they develop a "fear of the pot." They seem to prefer to defæcate in the standing position, and they stiffen knees and hips and lie back in supine position if forced to use the pot; presumably this position affords them the least discomfort in the act of defæcation. The fear of the pot, the soiling of the hands and clothes due to overflow incontinence, and their natural shame about these unpleasant features are rapidly and completely eliminated by physical treatment of the constipation and therefore do not appear to be psychogenic. The benign course of this condition is also illustrated by the fact that no children in this group have died.

RADIOLOGY

Of the 73 cases in the series 71 were investigated radiologically. Of 61 of these, investigated with barium enema by one of us (B. C. H. W.), 26 had old films which could be reviewed. In the remaining 10 cases only films taken at previous examinations were available.

No routine preparations, such as bowel washouts and purgation, were made before the enemas. To avoid the sequelæ of desiccated barium in the colon, glycerin and paraffin were introduced into the barium emulsion. This was run into the bowel, from an initial height of 3 ft. above the table, through a soft rubber catheter introduced a minimal distance into the rectum. The flow was under the immediate control of the radiologist, and the initial filling of the rectum and rectosigmoid region was closely observed. The enema was stopped as soon as diagnosis could be made; thus none of the abnormal colons were examined in their entirety, and the possibility of dilatation from continued high hydrostatic pressure was minimised.

The flow of the enema was stopped at various stages of filling, and postero-anterior, lateral, and oblique films were taken in such positions as would best show the abnormalities and the rectosigmoid region. Films were also taken immediately after evacuation. The effectiveness of these initial attempts of evacuation showed no variation between the various groups and is probably of no significance. It was impossible in most cases to take films at a twenty-four hour interval.

Group I: Hirschsprung's Disease

The findings were characteristic of Hirschsprung's disease in 34 cases: in 2 other children, aged fifteen days and eleven weeks, clinically diagnosed as having acute Hirschsprung's disease, death took place before a certain radiological diagnosis could be made, and in 1 case of chronic Hirschsprung's disease the old films did not fulfil all the radiological criteria. All these patients belonged clinically to group I.

In the chronic stage the straight film of the abdomen shows gross gaseous distension, with the ribs splayed and the distended colon immediately below the diaphragm on both sides. As the flow of the barium enema is watched, it is seen to fill the rectum, which appears to be of normal or less than normal size. Above the rectum the diameter of the gut narrows for a distance which varies greatly from case to case (about 1–12 in.). Above this it opens by a wide funnel into hugely dilated and gas-filled colon (figs. 1 and 2). There the emulsion can be tipped round the colon and fluid levels demonstrated. Once this dilated portion is filled, the narrowing below may be obscured and very difficult to demonstrate.

When the narrow segment was long enough to be well seen, the bowel wall had a rippled appearance, and in 3 cases segmentation of the column of barium, such as is normally seen in the small gut, was noted. Low spinal anæsthesia was induced in these 3 cases and the enemas were repeated. The outline of the narrow segment

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was then shown to be smooth, inactive, and slightly wider. There was, however, no spontaneous evacuation, the enemas being well retained.

In 2 children aged less than one year, the first examination showed no dilatation. The rectum and the distal colon appeared rather small, and 1 case showed the rippled outline and segmental movement. At subsequent examinations dilated colon was found above a narrowed segment. In these and other early cases the dilatation was confined to the portion of colon immediately proximal to the narrowed segment. At each further examination the dilatation was shown to extend further towards the cæcum.

In 3 cases the patients were examined after excision of the dilated portion of colon (the distal pelvic colon; the left half of the colon; the whole colon). The undilated colon or the ileum had then been anastomosed to the distal sigmoid segment. All the cases now showed a narrowed distal segment with dilatation proximally. In the child whose entire colon had been removed, the

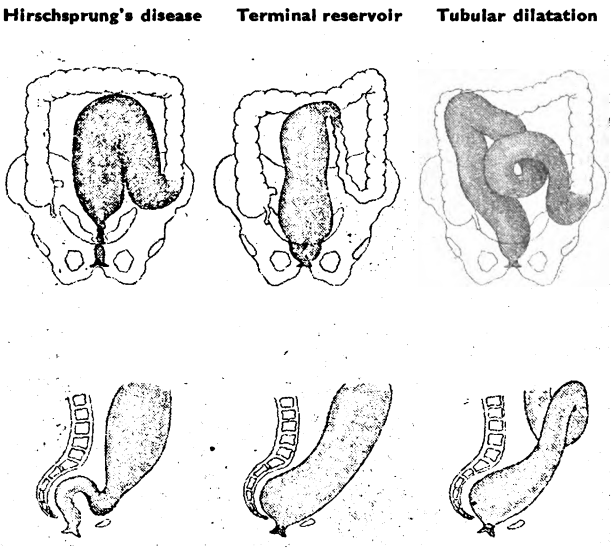

Fig. 1—Radiographic appearances.

distal ileum, because of its size and situation, could have been mistaken for megacolon.

Group II: Idiopathic Megacolon

Of the 34 cases 22 showed simple colonic dilatation. They fell roughly into two subgroups: (1) in 10 the distension was confined to the rectum and distal pelvic colon, forming a "terminal reservoir" (fig. 1), and (2) in 12 "tubular dilatation" (fig. 1) of a longer segment was noted.

When a *terminal reservoir* is present, a straight film of the abdomen may show a portion of dilated gas-filled gut, and barium enema shows that the rectum and distal pelvic colon form a pear-shaped unilocular dilated chamber extending in some cases from the anus to xiphisternum. Unless there has been special preparation, this chamber contains large fæcal masses. Proximal to this the colon returns largely to normal diameter.

With *tubular dilatation* the rectum appears large, and the pelvic colon, which is longer and wider than usual, lacks haustration; but the contour of the bowel is otherwise normal. The boundary between normal and abnormal bowel is ill defined. Fæcal masses are commonly present, but gaseous distension is minimal.

The remaining 12 cases, at their final and usually recent examination, were radiologically classified as apparently within the range of normality. All these 12 cases had been diagnosed as megacolon or Hirschsprung's disease. Clinically we now regard them as belonging to group II.

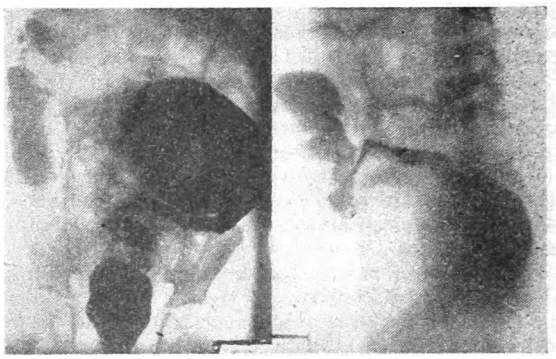

Fig. 2—Anterioposterior and lateral radiograms after barium enema in Hirschsprung's disease with long narrow segment.

PATHOLOGY OF HIRSCHSPRUNG'S DISEASE

Our lack of knowledge of the ætiology of idiopathic megacolon is implied by the term "idiopathic." Failure to find a generally acceptable solution has been due to two main misconceptions: (1) that all cases of idiopathic megacolon are Hirschsprung's disease; and (2) that the dilated bowel is the site of the primary disorder.

Two previous conceptions of the ætiology have been discarded—namely, the malformation theory, which postulates congenital giant growth of colon; and the obstruction theory, which assumes redundancy and kinking of part of the colon. A third, the neurogenic theory, has been largely based on the assumption of functional autonomic imbalance.

Neurohistological investigations have produced contradictory results. With few exceptions, there is agreement that sympathetic ganglia, removed surgically in cases of megacolon in childhood, are histologically normal; but there is no such agreement on the parasympathetic histology.

Brentano (1904), Finney (1908), Schmidt (1909), Retzlaff (1920), and Pässler (1938) could not find any abnormalities in the autonomic innervation of the bowel, but they examined the dilated bowel only.

Tittel (1901), Cameron (1928), and Robertson and Kernohan (1938) claimed to have found scantiness, degeneration, or absence of ganglion cells. Since their examinations were very limited, we do not propose to assess their results.

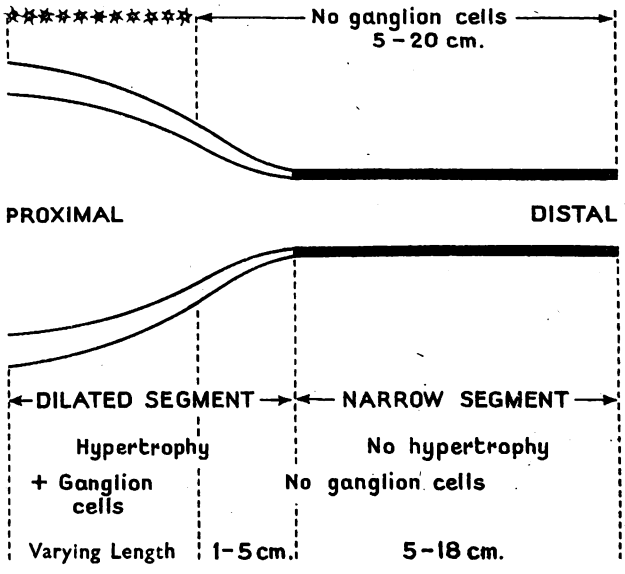

Fig. 3—Pathology of 15 cases of Hirschsprung's disease with narrow segment.

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Dalla Valle (1920, 1924) reported megacolon in two siblings with absence of ganglion cells in the sigmoid colon and normal ganglia in the proximal bowel. They do not report on examination of the rectum.

Perrot and Danon (1935) described intestinal obstruction with no demonstrable organic cause in an infant aged fifteen days. Scantiness of ganglion cells was claimed from the terminal ileum to the splenic flexure, with normal ganglia above and below this segment. We have no cases showing merely reduction in numbers of ganglion cells.

Tiffin et al. (1940) reported a case, in an infant aged twenty months, with localised aplasia of ganglion cells in 5–7 cm. of proximal sigmoid colon, and normal ganglia above and below. We have not observed any isolated segmental aplasia of ganglion cells between normal portions of bowel.

Zuelzer and Wilson (1948) have reported complete aplasia of ganglion cells from the myenteric plexus in the distal segment in 5 infants, aged from eleven days to two months. All 5 presented with acute intestinal obstruction. In addition they describe segmental aplasia of ganglion cells in an excised colostomy loop in a child who survived to the chronic stage of intestinal obstruction. They also observed well-developed ganglion cells at every level of the intestine in 10 controls and in 2 cases of "typical megacolon."

(We are not citing Etzel (1937) and other South American workers who described acquired megacolon in adults.)

The work done by one of us (M. B.) on the neurohistology of megacolon has been greatly helped by the

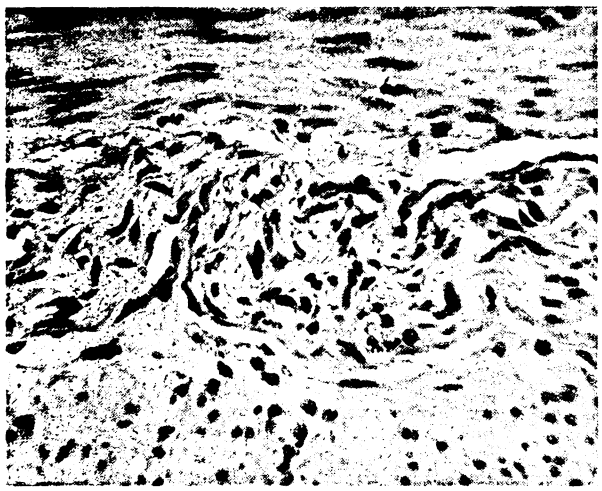

Fig. 4—Intramural plexus in narrow segment in Hirschsprung's disease, showing absence of ganglion cells. (× 300.)

clinical and radiological division into two main groups, and was concerned with group I, or Hirschsprung's disease, only.

Material.—Our material consisted of 15 specimens. The first 2 were derived from necropsies done in 1947. Of these 1 was from an infant, aged fifteen days, presenting with acute intestinal obstruction with no demonstrable organic cause. The intestine from terminal ileum to splenic flexure was moderately dilated but not hypertrophied, and the intestine below the splenic flexure was normal in diameter. The remaining 14 specimens came from children, aged from eighteen months to thirteen years, with chronic Hirschsprung's disease. Of these 1 died in 1947, four days after total colectomy. Another specimen was an excised sigmoid colostomy loop (1947), and the remaining 12 were surgical specimens removed by rectosigmoidectomy (F. D. S.) in the latter half of 1948.

Findings.—Blocks were examined from consecutive levels of both mesenteric and antimesenteric aspects of the entire intestinal tract in the 2 specimens obtained at necropsy and of the complete surgical specimens. The pathological findings in both intramural plexuses (myenteric or Auerbach's, and submucous or Meissner's) were uniform in all 15 specimens; complete absence of

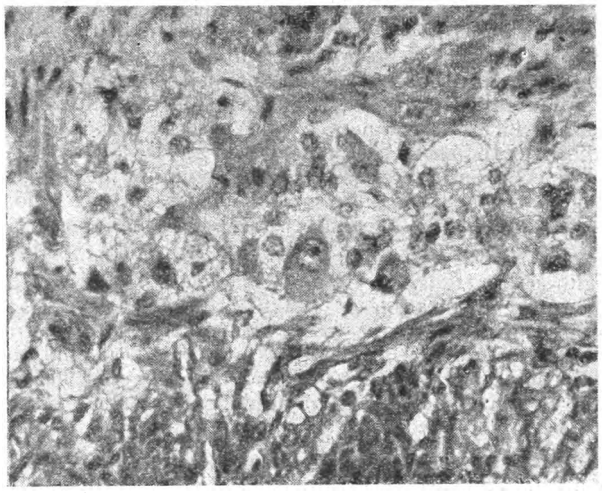

Fig. 5—Intramural plexus in dilated segment in Hirschsprung's disease, showing normal ganglion cells. (× 280.)

parasympathetic ganglion cells was noted throughout the entire narrow segments, which were 5–18 cm. long (fig. 3). Moreover, these aganglionic segments extended beyond the narrow bowel into the dilated part for 1–5 cm. The plexuses in the pathological segments consisted of numerous bundles of nerve fibrils (presumably sympathetic in origin) and interstitial cells (fig. 4). These bundles were much denser in the pathological segment, in contrast to their rather vacuolated appearance in the normal portion of bowel (fig. 5). No inflammatory changes of significance were noted in the plexuses, and we do not think that the absence of ganglion cells can be due to inflammation. It cannot be stated with certainty on histological grounds alone whether this lesion resulted from degenerative changes. Circumstantial clinical evidence, however, strongly suggests a congenital lesion, and the histology is compatible with the assumption of an agenesis of ganglion cells.

The length of the segments varied considerably, some including rectum only, others rectum and rectosigmoid colon, and some, in addition, a varying portion of sigmoid colon. The longest segment observed by us came from the infant with acute intestinal obstruction in whom no ganglion cells were found in the intestine distal to the splenic flexure.

Proximal to the pathological segments, ganglion cells were perfectly normal, though somewhat scantier in the immediate transition zone.

All these pathological findings were assessed against the background of a comparable control series which consisted of eleven specimens of sigmoid colon, rectum, and anus. Numerous ganglion-cell groups were found at close spacing (every 1–5 mm.) throughout the entire segment down to 3–15 mm. from the anocutaneous junction.†

PRESENT TREATMENT OF HIRSCHSPRUNG'S DISEASE BY RECTOSIGMOIDECTOMY

Procedures adopted in the Hospital for Sick Children, have been based on the observations of Swenson and Bill (1948) at the Boston Children's Hospital. These workers conclude on clinical and radiological grounds that the narrow spasmodic segment is the obstructing factor, and they have concentrated their efforts on this group of cases. They removed this segment by the pull-through technique, with preservation of the sphincter, and have now treated many cases successfully in this way.

† Since this report was written 2 further cases of Hirschsprung's disease have had rectosigmoidectomy performed. The histological findings were the same.

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Our treatment embodies the principles suggested by Swenson and Bill but varies in some points of technique adopted to render the procedure more speedy and clean, and to reduce postoperative bladder disturbances to a minimum. The term "rectosigmoidectomy" can be applied in most instances to this procedure, but would not cover the cases with longer segments.

We consider it safer to do the operation in four stages, though we realise that some mild cases with short segments could be adequately treated in one stage.

Stage 1.—Defunctioning of the distal colon by a right-sided transverse spur colostomy, followed by thorough preparation of the distal segment. It has been considered wisest to leave an interval of several months before the next stage is attempted, so that the child may increase in weight and improve in health, and so that œdema and glandular enlargement in the mesosigmoid may be given time to subside.

Stage 2.—An abdominoperineal rectosigmoidectomy is done. The special features associated with this operation, as distinct from the usual technique adopted in cancer surgery, are as follows:

(1) Delineation of the abnormal segment. The proximal end of the thin-walled narrow segment can be determined at its junction with the cone-shaped hypertrophied and dilated bowel. If this junction is situated at a low level in the true pelvis it is sometimes difficult to find at operation.

(2) The site of election for proximal resection of the bowel is about half-way along the cone-shaped funnel, since we have found that the ganglion cells usually disappear there.

(3) The rectum is dissected from its supporting fascia propria distally as far as the levator ani muscle. This is aimed at reducing interference with bladder innervation.

(4) The narrow segment is totally intussuscepted out of the pelvis through the anus.

(5) The prolapsed segment is then excised, leaving about $^1/_2$ in. of anal canal to which the cone-shaped portion of colon is anastomosed.

Stages 3 and 4.—These consist of crushing of the spur and closure of the colostomy.

The essential differences between our technique and that described by Swenson and Bill consist in: (1) resection of the bowel after intussusception, instead of intra-abdominal division, before intussusception and resection; and (2) the careful dissection of the rectum from the fascia propria.

SHORT-TERM RESULTS

Of the 12 cases which have undergone rectosigmoidectomy, 11 have now been completed for periods ranging from one week to three months, and 1 awaits closure of the colostomy.

In these 11 cases the bowels now act regularly, without constipation, abdominal distension, or incontinence. Motions still tend to be of small diameter, like toothpaste, and soft. It is conceivable that this results from there still being a residual short pathological anal segment (about $^1/_2$ in. long).

There has been no death in this series. In 5 cases complications arose: 3 had postoperative retention of urine, which quickly subsided, except in 1 case, which is only now improving after a month (alterations in the technique of dissecting the rectum from the fascia propria, instead of removing the fascia with the rectum, may possibly explain the absence of this complication in the last few cases); 1 child had a mild form of narrowing at the anastomotic site, which was easily dilated per rectum with the finger; and 1 had a minor degree of incontinence but has responded satisfactorily to training.

DISCUSSION ON HIRSCHSPRUNG'S DISEASE

Certain clinical features indicated that the distal narrow segment was the site of intestinal obstruction, and that dilatation and hypertrophy of the bowel proximal to it were secondary phenomena:

(1) Colostomy proximal to the narrow segment alleviated the symptoms immediately, and the colostomy functioned normally.

(2) Attempts at closure of the colostomy were often unsuccessful.

(3) Symptoms and signs recurred after successful closure of the colostomy.

(4) Excision of part, or the whole, of the dilated colon was followed by relapse of all the symptoms and reappearance of dilatation and hypertrophy of the intestine proximal to the site of anastomosis to the narrow segment.

(5) Spontaneous bowel action followed rectosigmoidectomy as judged in a short-term follow-up.

Disappearance of haustration and slight dilatation of the distal segment under spinal anæsthesia are interpreted as radiological evidence supporting a spastic obstructive factor.

Pathological evidence of structural changes in the parasympathetic innervation of the distal segment explains the lack of its coördinated propulsive movement. The unopposed action of the sympathetic nerves explains the spastic factor.

We have tried to correlate the degree of intestinal obstruction, as measured by the degree of constipation, with the length of the obstructing segment. However, the degree of constipation varied considerably in individual cases during the course of the disease, and we assume that factors other than the length of the pathological segment must be responsible for this variation. Transient impaction of fæces in, and kinking of, this segment may be two such additional factors.

SUGGESTED MANAGEMENT OF GROUP II (IDIOPATHIC MEGACOLON)

The management of these cases embodies three principles:

(1) *Thorough and repeated evacuation of the bowels.*—If the rectum is firmly impacted with hard fæces, these must be removed by hand under general anæsthesia. If the fæces are soft, bowel lavage is adequate. Colonic lavage is required daily until all fæcal masses are removed, and subsequently three times weekly for three weeks and twice weekly for two weeks. It is important to continue this treatment even if bowel actions become normal. Thereafter, weekly bowel washouts are given for a varying period according to the response.

(2) *Purgation.*—After removal of the main bulk of fæces regular treatment with purgatives is initiated.

(3) *Education in normal bowel habits.*

SUMMARY

An analysis of 73 cases of idiopathic megacolon is reported, excluding cases of symptomatic megacolon with demonstrable organic cause; 39 cases conformed to Hirschsprung's clinical pattern. A narrow distal segment of intestine was demonstrated in 34 of these cases by special radiological technique, and in 5 at necropsy only.

Neurohistological investigation of a consecutive series of 15 cases of Hirschsprung's disease (diagnosed clinically and radiologically) revealed the absence of parasympathetic ganglion cells from the intramural plexuses of the narrow intestine and a small adjoining segment of dilated colon.

This suggests a uniform pathology in Hirschsprung's disease, accounting for the lack of parasympathetic function—i.e., coördinated propulsive movement of the distal segment. Unopposed sympathetic activity accounts for spasm in the distal segment.

This distal colonic obstruction leads to secondary dilatation and hypertrophy in the bowel proximal to it.

A scientific basis is thus offered for the treatment of Hirschsprung's disease by rectosigmoidectomy.

A considerable proportion of cases of megacolon (not being Hirschsprung's disease) remain in the residual

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"idiopathic" group. They display a characteristic clinical picture and two types of radiological pattern (terminal reservoir and tubular dilatation), and are probably of miscellaneous ætiology. A scheme of prolonged conservative treatment is suggested.

We wish to acknowledge, gratefully, the coöperation of the consultant staff of the Hospital for Sick Children, Great Ormond Street, particularly of Mr. Denis Browne, who has contributed largely towards simplifying the surgical procedure. One of us (F. D. S.) had the good fortune to visit Dr. Orvar Swenson of the Boston Children's Hospital, in 1947, and it was there that our surgical interest in the subject was stimulated. We are indebted to the Nuffield Foundation for their great interest in the work, and for their grant to F. D. S. It gives us great pleasure to thank Mr. Derek Martin and the photographic department for their tireless efforts in collecting records, some of which are included in this paper. Our thanks are also due to Mr. V. C. Conlay and his staff for numerous histological preparations. We are no less indebted to many more who cannot be mentioned personally.

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INTRAVENOUS TREATMENT OF ANÆMIA WITH AN IRON-SUCROSE PREPARATION

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MOST patients with iron-deficiency anæmia respond satisfactorily to adequate doses of iron preparations by mouth, but some, though free from the complications of neoplasm, chronic infection, thyroid deficiency, &c., do not respond to large doses of both ferrous and ferric iron by mouth, even when the iron is well tolerated. There is also a larger group of patients who suffer such gastro-intestinal upset from the administration of iron preparations by mouth that they cannot take enough to relieve the anæmia satisfactorily.

There have been many attempts to find a satisfactory iron preparation suitable for parenteral administration. The older work was reviewed by Stockman (1893). Small amounts—i.e. 10–20 mg. of elemental Fe daily—have often been given in the form of ionised iron compounds such as ferric ammonium citrate, ferrous gluconate, ferrous ascorbate, and ferric hydroxide. In all cases the intramuscular route proved too painful, and more than 10–20 mg. of elemental iron given intravenously produced severe heavy-metal intoxication. Goetsch et al. (1946) introduced 0·608–1·32 g. of elemental iron as colloidal ferric hydroxide intravenously into 8 patients with iron-deficiency anæmia. The hæmatological responses were dramatic, but these workers concluded: "There can be no doubt that the reactions to iron parenterally administered in large doses are great enough to contra-indicate use of this measure as a therapeutic procedure." Nissim (1947) reported the successful treatment of a few patients with iron-deficiency anæmia with large intravenous doses of a saccharated-iron preparation. The reactions he encountered were less severe than those reported by earlier workers, but the ferri ox. sacch. *B.P.* that he used was and is a variable product, and he concluded that "the uniform production of a safer variety would be a further step forward."

Since 1930 we have been interested in the possibility of producing a preparation of iron that could be given safely and effectively, either intramuscularly or intravenously, to these patients with iron-deficiency anæmias. Many preparations have been tried intramuscularly in doses containing 7–50 mg. of elemental iron. In all cases the injections were so painful that it was impossible to give more than 320 mg. of iron in sixteen days. Our clinical results with certain iron preparations given intravenously are reported here.

We devised a simple serum-compatibility test to act as a preliminary in-vitro screening test for a large series of iron preparations and compounds. This test is carried out as follows:

To 5 ml. of fresh human serum 0·1 ml. of the solution of the iron compound to be tested is added drop by drop with shaking, and the whole mixture is allowed to stand at 37°C for an hour, when it is examined by naked eye and under low-power microscope for evidence of flocculation.

Simple ionic compounds cause immediate protein coagulation, but only a fine flocculation or a slight gel is formed by colloidal ferric hydroxide (0·5% Fe), ferrous gluconate (1% Fe), sodium ferrous lactobionate (1·7% Fe), and sodium ferric mucate (1·9% Fe). Two compounds give no flocculation, cloudiness, or gel and appear to be completely compatible with serum: these are iron diammonium chelidamate (1% Fe) and seitz-filtered ferri ox. sacch. *B.P.* (1% Fe).

In a trial of these six compounds by intravenous injection, done early in 1947, classical symptoms of iron intoxication appeared after the injection of amounts equivalent to 10–20 mg. of elemental iron, except with the seitz-filtered ferri ox. sacch.; this last preparation was therefore studied more closely.

"SACCHARATED IRON"

In an experimental study of the effects of iron compounds on the reticulo-endothelial system in animals Cappell (1930) noted that "saccharated oxide of iron" was much better tolerated than colloidal ferric hydroxide, but the commercial product was very variable, giving either clear brown solutions that appeared to be well tolerated or cloudy flocculent liquids that were tolerated less well. We found that sterilising these solutions by autoclaving invariably produced opaque cloudy suspensions or even precipitation. Seitz-filtration, however, usually gave a fairly satisfactory product suitable for intravenous injection.

Mannich and Rojahn (1922), who had studied the properties of "saccharated iron," concluded that "saccharated iron" was a negatively charged colloidal solution of "iron oxyhydrate," which was stabilised by adsorption of alkali and sugar. We repeated the experiments on which this conclusion was based and fully confirmed their results. It was also noted that with a lowering of the pH the colloid reverted from the sol to the gel phase but that this was reversible in certain circumstances.

Attempts to prepare a satisfactory compound from existing commercial supplies had entirely failed, and the reaction was studied with the following analytical grade reagents as a starting-point: anhydrous ferric chloride, sodium carbonate, sucrose, and sodium hydroxide. From a long series of experiments we concluded that (1) the pH was a critical factor, (2) the reaction time was equally important, in that the time-temperature factor controlled the extent and rate of fall of pH resulting from acidic thermal breakdown products of the sucrose, and (3) some

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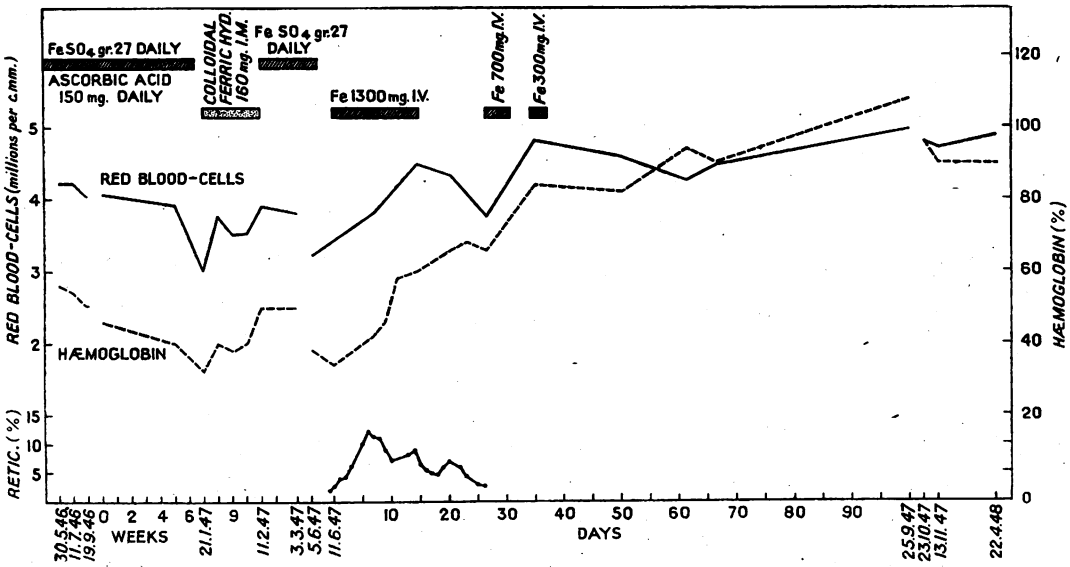
sodium carbonate was essential—possibly the colloid could only be formed from ferric subcarbonate. Attempts to obtain a stable negatively charged colloid from colloidal ferric hydroxide failed. The final preparation as we made it was as follows:

Anhydrous ferric chloride (5·8 g.) is dissolved in distilled water (50 ml.) in an evaporating-dish on a water-bath at 95°C, and sucrose (28 g.) is added with stirring until dissolved. Dissolve anhydrous sodium carbonate (1·8 g.) and sodium hydroxide (5 g.) separately in 25 ml. of water each. Add slowly the carbonate solution to the ferric chloride solution, stirring well and allowing the carbon dioxide to come off after each addition. Now add the sodium hydroxide solution, stir well for 15 min., and filter through a Whatman no. 42 filter paper into rubber-capped vials or ampoules; autoclave immediately at 115–116 lb. per sq. in. for 20 min.

After autoclaving, we invariably obtained a clear dark-brown solution of about pH 10·5, which remained stable at room temperature for at least twelve months. This solution contains 2% elemental iron.

This iron-sucrose preparation has been given intravenously in repeated doses for therapeutic or experimental purposes to over 120 people, but here we are concerned only with the hæmatological responses of the first 60 patients with iron-deficiency anæmia. About a third of these have been treated with the preparation as described above, and the remainder have had another form of iron-sucrose preparation, 'Ferrivenin,' supplied by Benger's Ltd. There has been no detectable difference in tolerance or response in very many batches of either of these two preparations.



Achlorhydric iron-deficiency anæmia (case 5) refractory to iron by mouth and treated with intravenous iron-sucrose preparation.

TECHNIQUE OF ADMINISTRATION

Dosage.—Cappell (1930) had noted a rapid increase of tolerance to saccharated iron given intravenously to mice and rabbits. Nissim (1947) also found increased tolerance in man after gradually increasing the dosage. We have also observed this.

The total iron required in this series was calculated from the data of Roscoe and Donaldson (1946) for women and of Davis (1942) for men, the surface area being obtained from the height and weight of Du Bois' tables and hæmoglobin assumed to contain 0·34% of iron. Obtained in this way the figures are approximate only, and percentage utilisation of the iron can be judged with reasonable accuracy only if the administered dose is on the low side of individual requirement. Since, however, the body's iron stores are also depleted in iron-deficiency anæmia, the most satisfactory total dose proved to be the calculated deficit plus 50%. For ordinary routine outpatient treatment it is sufficient to base the required total dose on 24·5 mg. of elemental Fe for each 1% deficit of hæmoglobin (as determined on the Haldane scale), plus 50%.

Our scheme of dosage finally adopted was 25 mg. on the first day, 50 mg. on the second, 100 mg. on the third, and 200 mg. on the fourth and subsequent days, but occasionally patients had 200 mg. twice daily with an interval of six hours. In many of the 60 cases reported here the total dose given was deliberately within the calculated deficit so that we could study utilisation; consequently the final hæmoglobin levels were not always so high as those obtained with fully adequate therapy. On the other hand, some of the patients received the full dose as just outlined, and no recurrences have been observed in them, but the longest period of observation is at present only some eighteen months.

Injection Technique.—The iron-sucrose preparation was given from an all-glass 5 or 10 ml. syringe with no. 2 stainless-steel 'Record' needles into antecubital veins at the rate of about 2 ml. a minute. The solutions contained 2% elemental iron, and a 200 mg. dose was therefore contained in 10 ml. No follow-on lavage of the vein was required, provided that the same vein was not used on consecutive days. Four small thromboses only were encountered in this series of over 700 separate injections. Intravenous infusions of 500 mg. of Fe each were given on a few occasions, but mild iron intoxication developed, and there was no advantage in using this relatively laborious method.

REACTIONS

With the above-mentioned scheme of dosage only 1 of 60 patients developed mild reactions at the 200 mg. level. All the other patients tolerated 200 mg. daily, or twice daily, without any reactions. Larger single doses, such as 300 mg., cause mild reactions in many patients and should not be used. The treatment was usually completed in 10 outpatient visits or less if 200 mg. doses were given twice daily. The patients did not require to rest after the injection.

Most of our 60 patients were outpatients attending our clinics in the Department of Hæmatology, Manchester Royal Infirmary, but some were admitted to the wards of this hospital for special investigations and other treatment. All had from moderate to severe iron-deficiency anæmias as manifested by a low colour-index anæmia, low M.C.H. and M.C.H.C., lowered plasma-iron level, and the usual classical symptoms of iron-deficiency anæmia.

Of these 60 patients, 10 had proved refractory to full doses of iron by mouth over long periods (see figure). It

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TABLE I—SUMMARY OF CLINICAL AND LABORATORY FINDINGS IN 60 PATIENTS WITH IRON-DEFICIENCY ANÆMIA

Age-groups (yr.)			Sex		Nutrition		Skin		Nails		Tongue		Gastric acidity						Causes						Hæmoglobin (%)			Plasma-iron (µg. per 100 ml.)				
Under 20	20–50	Over 50	Male	Female	Good	Poor	White or waxy	Yellowish	Koilonychia	Brittle	Glossitis	Normal	Dysphagia	Flatulent dyspepsia	Achlorhydria	Hypochlorhydria	Normal acidity	Unknown	Menorrhagia	Pregnancy	Intestinal bleeding	Dietetic	Refractory to iron by mouth	Chronic infection	20–50	50–70	70–80	0–20	20–40	40–60	60–80	Unknown
1	52	7	3	57	56	4	54	6	8	28	28	32	3	40	31	6	13	10	19	7	10	12	10	2	24	30	6	19	20	11	8	2

AVERAGE VALUES

Age (yr.)	Sex (%)	Achlorhydria (%)	Initial Hb (%)	Total iron given (mg.)	Hb increase (%)	Iron utilised (%)	Daily rate of increase of Hb at 21–35 days (g.)			Plasma-iron (µg. per 100 ml.)
							All cases	First 18	Last 42	
43	95 ♀	52	50	920	36	98	0·184	0·121	0·215	32

is impossible to be certain, with our present knowledge of iron metabolism, that failure to absorb iron from the intestinal tract was the essential cause in these patients. All were women aged 20–50. In none was there any evidence of excessive blood-loss from the body, but all had a past history of pregnancy and a variable degree of menorrhagia. It seems that the impaired iron absorption was a later phenomenon, preventing repair of the anæmia, rather than the original cause. In 38 patients iron-deficiency anæmia developed after severe menorrhagia, pregnancy, and inadequate diet. In many of these 38 cases these causes were concurrent as a triad, but one or other would predominate in any given case, as indicated in table I.

The number of iron deficiencies resulting from intestinal bleeding was 10: hæmorrhoids 2; pernicious anæmia and chronic intestinal bleeding of unknown cause 1; inoperable carcinoma of the stomach 1; thrombocytopenic purpura 1; chronic intestinal bleeding of unidentified cause 1; and chronic mucous colitis 4. Of 2 patients with chronic infection, in neither of whom was there at any time any demonstrable blood-loss, one had spinal caries and the other rheumatoid arthritis.

The clinical and hæmatological findings in these 60 cases of iron-deficiency anæmia and their response to intravenous iron-sucrose are summarised in tables I and II.

Hæmoglobin estimations were done with a Haldane hæmoglobinometer standardised by the National Physical Laboratory. A modification of the method of Kitzes et al. (1944) was used for plasma-iron determinations—an αα dipyridyl method using a Spekker absorptiometer and spectrum green filter (Ilford 604). Our range of normal plasma-iron values for this method was 142σ 23·8 µg. per 100 ml. in men and 117σ 30·5 µg. per 100 ml. in women.

RESPONSE TO TREATMENT

The experience gained in eighteen months in treating these 60 patients with iron-deficiency anæmia and other patients has shown that in these iron-sucrose preparations we have a relatively safe and effective vehicle for giving iron parenterally. Reactions, if any, were mild, and the incidence of even small local venous thromboses has been very low—only 4 in over 800 injections. The response to treatment was initially good in 57 of these 60 cases.

In almost all the patients there was a rapid and complete amelioration of such classical symptoms of anæmia as dyspnœa, palpitations, tiredness, loss of appetite, and dyspepsia, and a more gradual but equally complete return to normal nail formation. There was striking and permanent improvement in 2 of the 3 patients with Plummer-Vinson syndrome, but in 1 the dysphagia remained unrelieved. The hæmatological and clinical responses were often as dramatic as those obtained when patients with pernicious anæmia in relapse receive adequate doses of a potent intramuscular liver extract. In these cases a reticulocyte peak of 10–18% developed seven to ten days from the beginning of the

TABLE II—RESPONSE OF 60 CASES OF IRON-DEFICIENCY ANÆMIA TO INTRAVENOUS IRON-SUCROSE PREPARATION

Case no.	Before treatment								Total dose I.V. Fe (mg.)	I.V. Fe utilised (%)	After treatment									
	Age (yr.)	Red cells (millions per c.mm.)	Hb (Haldane) (%)	Plasma Fe (µg. per 100 ml.)	Hæmatocrit	M.C.H. (µµg.)	M.C.H.C. (%)	Calculated Fe deficit (mg.)			Day after 1st treatment	Red cells (millions per c.mm.)	Hb (%)	Day after 1st treatment	Red cells (millions per c.mm.)	Hb (%)	Day after 1st treatment	Red cells (millions per c.mm.)	Hb (%)	Plasma-iron (µg. per 100 ml.)
1	38	3·12	48	32	34	21	20	1360	1285	98	99	4·71	96	176	5·14	102	281	5·22	100	..
12	50	4·48	46	17	29	14	22	1295	1200	106	37	5·18	80	79	5·62	100	282	4·92	90	116
18	25	4·77	54	24	34	15	22	1150	1100	103	13	5·22	80	46	5·38	101	168	5·56	104	98
37	43	4·25	42	63	34	13	17	1450	1050	107	20	5·18	88	44	4·56	90	100	5·17	96	128
51	43	4·42	70	10	37	22	26	800	675	90	29	4·80	88	43	4·81	84	79	5·10	94	32
56	40	4·08	62	Nil	..	..	..	900	825	96	14	4·32	82	21	5·36	90	28	5·15	92	52

The above six cases are a selection of the table which considerations of space prevent printing in full. The complete figures are available on request from THE LANCET. The cases are in chronological order; case 1 began treatment on May 15, 1947, and case 56 on March 10, 1948.

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intravenous iron therapy. Clinically the earliest improvement noted was a return of appetite at about forty-eight to seventy-two hours, for in many of them loss of appetite had been a salient feature. This improvement of appetite and of digestion has been well maintained. Of these patients 4 with chronic mucous colitis all showed a rapid improvement in bowel action within the first seventy-two hours, with a reduction from 12 or more loose stools daily to 1 or 2 much better-formed stools. Unfortunately this improvement in the colitis has been maintained in 1 patient only, the other 3 having relapsed after two or three months, though maintaining normal blood-counts.

Utilisation of the intravenous ferric-sucrose preparation appears to be nearly 100%, the loss by urinary excretion being negligible. The amount of iron excreted in the urine in the twenty-four hours following the intravenous injection of 200–300 mg. of ferric-sucrose preparation was determined, and the observed maximal increase of urinary iron, even when the plasma-iron reached figures as high as 3635 μg. per 100 ml., was 0·12% of the amount injected. In this series no adjuvants, such as manganese, copper, cobalt, and molybdenum, have been used. When the need for iron exists, the hæmopoietic system appears to utilise to the full the ferric iron injected. The presence of carcinoma in 1 case, and of thyroid deficiency in 2 others, did not appear to prevent full utilisation. A man with hæmorrhoids received, after the reticulocyte percentages had returned to the base-line, ascorbic acid 500 mg. intravenously for six days and later folic acid 150 mg. without any observed effect on the rate of hæmoglobin regeneration or percentage of reticulocytes. Another patient received folic acid 20 mg. daily by mouth for seven days after the reticulocyte crisis, again with no effect on the rate of Hb regeneration or percentage of reticulocytes. Possibly, however, the correction of a proved vitamin-C deficiency in association with iron deficiency would lead to an increased rate of utilisation, but we have made no critical or extensive studies of this matter.

Utilisation is, however, seriously interfered with in the presence of chronic infection. This was found to be so in a patient with long-standing spinal caries and in one with active rheumatoid arthritis. The essential deficit in the patient with caries was 1250 mg. of iron, and he was given 950 mg. of iron with a good result, the Hb rising to 98% sixty-five days after the start of treatment. Four months later, however, he had relapsed, the Hb being 60% and the plasma-iron 56 μg. per 100 ml. He was therefore given a further 950 mg. of iron, and in twenty-seven days the Hb increased by 34% and the plasma-iron was 110 μg. per 100 ml. Whether he will again relapse remains to be seen. The patient with rheumatoid arthritis had a calculated deficit of 1550 mg. of iron; in all she received 2550 mg. of iron in three separate courses before there was a satisfactory response. Eighty-two days from the start of treatment the Hb increase was 48% (to 90%) and the plasma-iron had risen from 30 to 95 μg. per 100 ml. In neither case was there any question of blood-loss. It seems that in chronic infection there is a greatly increased demand for iron by the cell systems of the body, and that very large amounts of iron must be provided to enable the bone-marrow to obtain sufficient for its purposes and to maintain a normal plasma-iron level.

SUMMARY

A stable well-tolerated iron-sucrose preparation suitable for intravenous administration is described.

The technique of administration and scheme of dosage are indicated.

In 60 cases of iron-deficiency anæmia more than 800 intravenous injections of two forms of this preparation have been given in eighteen months.

This iron-sucrose preparation is an effective, safe, and easily administered form of parenteral iron, of great value in the treatment of iron-deficiency anæmia that has proved refractory to iron given by mouth, or of patients who do not tolerate iron by mouth in adequate doses.

The calculated iron deficit given in this manner is utilised almost quantitatively and does not appear to require the supplementary addition of trace elements, ascorbic acid, or folic acid.

We wish to thank Messrs. Benger's Ltd. for their help in preparing and supplying in quantity the iron-sucrose preparation ferrivenin, which we have given to some two-thirds of these patients.

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INTRAVENOUS IRON IN THE TREATMENT OF ANÆMIA OF PREGNANCY

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DIFFICULTIES in treating the common iron-deficiency anæmia of pregnancy by conventional methods are threefold: lack of time, intolerance of therapy, and, often, a lack of response to therapy.

In almost all cases time is a major problem. Most commonly anæmia manifests itself only in the later months of pregnancy; many patients have no symptoms of anæmia until the deficiency is gross; and often these patients present themselves for treatment only a week or two before term. In these cases iron by mouth is unsuitable and transfusion is the only available means of treatment.

Many pregnant women show a tendency to sickness and gastro-intestinal upset throughout pregnancy, and this is more pronounced in those with anæmia. Iron by mouth is not well tolerated, with the result that the response to treatment is slow. In some cases the slowness to respond is even greater owing to achlorhydria. For eighteen months in 1946–47, 900 women with anæmia of pregnancy were treated at the Glasgow Royal Maternity and Women's Hospital antenatal clinic. About 30% of these women had some gastro-intestinal complaint which made treatment difficult.

Refractory anæmias, showing little or no response to iron by mouth, are a common complication of pregnancy. Of the women just mentioned 20% did not respond satisfactorily to iron by mouth. About a quarter of these had pernicious anæmia of pregnancy, leaving 14·3% who appeared to have a simple iron-deficiency anæmia.

We have used 'Ferrivenin,'* a saccharated iron oxide intended for intravenous therapy, and the results have been very encouraging. Though it is too early to assess its true value in refractory cases, there is sufficient evidence that it is useful where time is short or the patient cannot tolerate iron by mouth.

We review here 25 cases treated with ferrivenin, and compare the response shown by patients given iron by mouth. During the first week injections were given daily, starting with a dose equivalent to 30 mg. of elemental iron on the first day, 60 mg. on the second day, and 100 mg. thereafter. At the end of a week injections were reduced to 100 mg. on alternate days.

* Manufactured by Benger's Ltd.

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RESULTS

The initial hæmoglobin (Hb) reading in these 25 cases was 16–60% (estimated by photo-electric colorimeter; 100% = 16 g. per 100 ml.): in 16 cases it was 40–50%; in 4 cases there was only moderate anæmia (Hb more than 50%); and in 5 cases the anæmia was very severe (Hb below 40%). In 3 of these last-mentioned cases the hæmoglobin was less than 30%. All the patients had the usual symptoms and signs of anæmia, the severity naturally varying according to the degree of anæmia. In addition many had trophic changes, such as glossitis, cheilosis, koilonychia, and œdema. In 2 cases iron had been given by mouth for three months without eliciting any response.

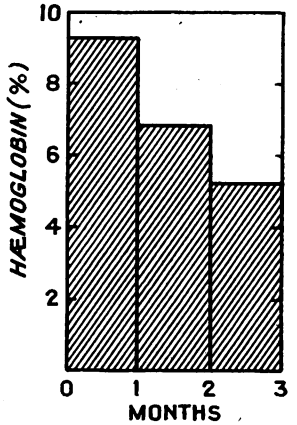

Fig. 1—Monthly increments of hæmoglobin in 21 patients with initial Hb. less than 50% and treated with iron by mouth.

According to the response to treatment the patients could be divided roughly into two groups—those in whom the Hb increased within four days after the equivalent of 290 mg. of iron had been given, and those in whom the response was delayed. About 60% of the patients showed an average increase of 5·7% (range 4–9%) of Hb after receiving 290 mg. of iron. By the end of a week, after 490 mg. had been given, the average Hb had increased by 8·2%.

The rate of progress varied inversely with the initial amount of Hb: below 40% the Hb increased by 2·4% per 100 mg. of iron given; and above 40% by 1·4% per 100 mg. of iron.

The initial reticulocyte response and the reticulocyte peak were also higher in patients with initial Hb below 40%. The highest reticulocyte response obtained was 16%. Where the initial Hb was above 50% there was very little reticulocyte response.

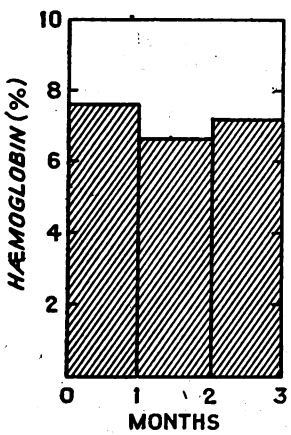

Fig. 2—Monthly increments of hæmoglobin in 41 patients with initial Hb more than 50% but less than 60% and treated with iron by mouth.

The following case-report is typical of the average patient:

An 8-para, aged 40, first attended the antenatal clinic on Sept. 17, 1948, when she was seven months pregnant. She was pale, but her mucosæ were moderately well coloured. She said she had been anæmic since the birth of her third child, when she had had a severe postpartum hæmorrhage. She now complained of feeling tired. Her appetite was poor and she was constipated. There was no sign of cheilosis or of koilonychia, but her tongue was dry and furred though not atrophic or fissured. Examination of her blood showed Hb 45%; red cells 3,760,000 per c.mm.; packed cell volume (P.C.V.) 26·5%; mean corpuscular volume (M.C.V.) 71·0 c.μ; mean corpuscular hæmoglobin concentration (M.C.H.C.) 27%; reticulocytes less than 1%; and plasma-proteins 5·1 g. per 100 ml.

Treatment with ferrivenin was started immediately, in the dosage described above. On Sept. 20, after the equivalent of 90 mg. of iron had been given, there was no change in the Hb, but there was a reticulocytosis of 3%. Blood examination on the day after the fourth injection of iron (Sept. 22): Hb 54%; red cells 3,740,000 per c.mm.; P.C.V. 30%; M.C.V. 80 c.μ; M.C.H.C. 29%; reticulocytes 4%; and plasma-proteins 5·7 g. per 100 ml.

By Sept. 25 the reticulocytes had increased to 9%, but the Hb had not increased further. On Oct. 4, after 990 mg. of iron had been given, the Hb rose to 58%, with red cells 3,880,000 per c.mm., P.C.V. 32·5%, and M.C.V. 84 c.μ; reticulocytes fell to 6%, and plasma-proteins to 5·3 g. per 100 ml. Just before the onset of labour on Oct. 15, the Hb was 70%, with red cells 3,910,000 per c.mm., P.C.V. 40%, M.C.V. 101 c.μ, and reticulocytes 1%.

In this case, therefore, the Hb had increased by 25% within 28 days, after an amount of ferrivenin equivalent to 1290 mg. of iron had been given. This represents an increase of 1·9% of Hb per 100 mg. of iron.

COMPARISON WITH IRON THERAPY BY MOUTH

To make a true comparison of these results with those obtained with iron by mouth, 62 cases of uncomplicated anæmia of pregnancy were selected from the large number treated by this method in 1946–47. These patients had no complaints other than those attributable to anæmia, such as breathlessness and fatigue. Of these patients 21 were severely anæmic, with Hb below 50%; the remaining 41 had Hb above 50% but below 60%. All of them were given 'Fersolate' gr. 15 daily. Figs. 1 and 2 illustrate the increase of Hb in the two groups during each month of treatment. Fig. 3 shows the weekly Hb increments in patients treated with ferrivenin and showing an immediate response. This group included the 2 patients whose anæmia proved resistant to iron by mouth. The difference between these graphs is very striking, not only as regards time but also because in the patients treated with ferrivenin succeeding increments of Hb increased, instead of diminishing as in the patients treated with iron by mouth. According to Whitby and Britton (1947) the response to iron by mouth varies inversely with the Hb level. This apparently does not hold with intravenous iron.

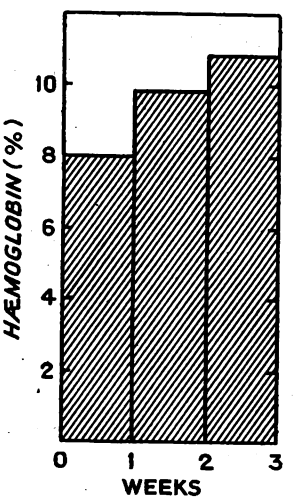

Fig. 3—Weekly increments of hæmoglobin in 15 patients treated with intravenous iron.

In 10 cases response was delayed. On the fourth day there was no increase in the Hb, and in 2 patients the Hb had decreased by 2%. There was, however, a reticulocyte response and the M.C.V. had increased. By the end of a week the Hb had increased by 3–7% in all the cases, and up to now no patient has failed to respond.

SYMPTOMATIC IMPROVEMENT

Though a reticulocytosis provided evidence of reaction on the part of the blood within a day or two, no change in symptoms took place until the patient's Hb had definitely increased. At this point the patient usually volunteered that she was feeling better and less tired. Her mucosæ generally showed a better colour. Within a few days, usually after 500–600 mg. of iron, the appetite improved and gastro-intestinal disorders, such as sickness, heartburn, constipation, and diarrhœa tended to disappear. Œdema also improved, but other trophic changes took longer to disappear. Cheilosis generally persisted until more than 1000 mg. had been given.

REACTIONS TO FERRIVENIN

The solution appears to irritate the vessel wall, and rapid injection causes an immediate venospasm. If,

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however, the solution is introduced gradually, there is no venospasm. About 10% of patients showed a slight general reaction to the first or second injection. Almost immediately after the injection the patient complains of a queer feeling which she cannot describe. She says her face feels swollen, and there is a definite suffusion of the complexion. The pulse is normal, and the reaction passes off in a few seconds. It does not reappear with further treatment

Only 1 patient showed a severe reaction. She had been irregular in attendance, and on one occasion she appeared twelve days after her previous injection, having had a total of 1690 mg. of iron intravenously. A few seconds after a further injection she complained of feeling faint and giddy, and this was followed by a sensation of fullness, almost of bursting, in the head, and sickness. Her face first became pale and then flushed. Beads of sweat appeared on the forehead, and her hands became moist. Her pulse-rate dropped from 80 to 40 and became very irregular, with extrasystoles, and her pulse became soft. The attack passed off within 2 or 3 min., and the patient appeared none the worse. No further intravenous iron was given to this patient. Her Hb was 69% at the time of injection, continued to increase during the next few days, and reached 73% a week later.

DISCUSSION

Cappell (1930) first showed that iron could be given intravenously as a saccharated iron oxide without the usual dangers attendant on the parenteral administration of other iron compounds. There appeared to be no danger of producing hæmochromatosis. This knowledge was not applied clinically, however, until Nissim (1947) reported that he had successfully treated anæmia by the intravenous administration of as table solution of saccharated oxide of iron. Davidson and Girdwood (1948), however, reported severe reactions following the use of a solution similar to that used by Nissim, but they supported his claim that it could improve the Hb level.

In the present series only one severe reaction was seen after the use of ferrivenin. It somewhat resembled anaphylaxis with vagal stimulation. It is possible that the patient's irregularity in attendance for treatment may be related thereto. The reaction to early injections in other patients was extremely mild and of no consequence.

Vannotti (1946) demonstrated the presence of radioactive iron in rabbits' red cells 2–5 days after its administration. This corresponds to the finding of a reticulocyte response within two days of the first injection of ferrivenin.

Several workers (Heath et al. 1932, Goetsch et al. 1946, Nissim 1947) have found that iron injected into non-pregnant anæmic women is used quantitatively, 24·5 g. of elemental iron being needed to increase the Hb by 1% a day. According to this scale 1 ampoule of ferrivenin, equivalent to 100 mg. of elemental iron, ought to increase the Hb by 4%. In our series, however, the highest response obtained was 2·6% per 100 mg. of elemental iron. The reason for this is not yet apparent. Perhaps some of the iron is deviated to the fœtus. We have found evidence that children born of anæmic mothers have insufficient stores of iron and often become anæmic during the first three months of neonatal life.

SUMMARY

Ferrivenin, a stable saccharated oxide of iron, has been given to 25 anæmic pregnant women.

All showed a rapid response to treatment, the hæmoglobin increasing, in almost all cases, by 8% in the first week of treatment.

The results are contrasted with those obtained with iron by mouth.

It apparently required almost 40 mg. of elemental iron to increase the hæmoglobin by 1% in an anæmic pregnant woman.

In 2 cases the anæmia was refractory to iron by mouth after prolonged treatment, but it responded satisfactorily to intravenous iron.

Only 1 case showed a severe reaction, which appeared to be due to vagal stimulation. This may have been related to the irregular attendance of the patient for treatment, there being an interval of twelve days between the previous injection and the date of the reaction.

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RESPONSE OF INFANTS TO DIPHTHERIA IMMUNISATION

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NATURAL antitoxic immunity against diphtheria has during the last decades decreased considerably in many parts of the world. As a result of extensive investigations von Groër and Kassowitz (1914, 1917, 1920) and Park and Zingher (1916) found immunity in about 85% of the adult population, but this figure is no longer valid.

Several factors have contributed to this decline. In many countries—e.g., Scandinavia—the incidence of diphtheria was low in the interval between the world wars, and hence the prerequisites for natural immunisation were limited. To some extent, however, the decrease in the number of immune persons has been fictitious. Some oft-cited earlier investigations showing a high percentage of immune persons concerned densely populated cities. The results of Park and Zingher (1916) in New York were no more representative of the diphtheria sensitivity of the population of the whole country than were von Pirquet's figures of tuberculin sensitivity in Vienna at the beginning of the present century. Kelly et al. (1925) found only 30·3% and 12·3% of students Schick-negative at two California colleges.

Zingher (1923) remarked: "In various city hospitals we have tested groups of nurses, many of whom had only recently come to the city from smaller communities, and have found that among them from 50% to 75% gave a positive reaction to the Schick tests." Subsequent workers have rarely noted this in referring to his work.

During the 1940's investigators in various countries published very low figures for the incidence of Schick-negative people. In Norway Ström (1942) found only 10·2% of 147 students Schick-negative. In Sweden Ericsson (1943) found 14% of 2274 conscripts Schick-negative. Similar figures were reported from Switzerland by Koller (1945). It can hardly be questioned that there has been a change for the worse in the general immunity to diphtheria. In England the incidence of diphtheria has until recent years been comparatively high. Nevertheless Wright and Clark (1944) found only 40% Schick-negative among 250 women recently delivered at a London maternity hospital.

The poor immunity of adults is reflected in infants. If women lack protective antibodies in their blood they cannot transfer a passive protection to their offspring. The old and still quoted rule that about 85% of all newborn infants are immune to diphtheria is no longer valid. In an investigation with antitoxin titrations on Swedish children (Vahlquist and Persson 1945) only 16% of the

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children under the age of 3 months had antitoxin in measurable amounts (≷ 0·0005 unit per ml. of serum).

It is therefore clear that in many parts of the world most infants completely lack antitoxic immunity against diphtheria. However, it is still probable that the risk of contracting diphtheria is lower in this age-group, for infants are relatively less exposed to infection and possibly possess a better "resistance" in their mucosæ. But, if they do contract the disease, the course is often malignant. In several local epidemics in Sweden among neonatal infants we have observed a mortality of 20%.

This change in the incidence of immunity suggests that newborn infants should be immunised to diphtheria. At present immunisation before the age of 6 months is usually discouraged because of the supposed passive protection. Apart from this it has been thought indisputable that the ability of the neonatal infant to produce antibodies is very poor (Blum 1932, McKhann and Kapnick 1938).

During the last few years I have been investigating passive and active immunisation against diphtheria in infants. The results have been reported in detail elsewhere (Vahlquist 1946, Vahlquist et al. 1948). The most essential results are shown in tables I, II, and III.

All of the immunisations were performed with aluminium-precipitated standard diphtheria toxoid, prepared according to Ericsson (1946), by the State Bacteriological Laboratory, its potency corresponding to 45 flocculation units per ml. The antitoxin titrations were performed by the method of Jensen (1933).

RESULTS

It is known that in naturally immunised persons the concentration of diphtheria antitoxin is the same in the newborn as in the mother. There is a priori every reason to assume that this also holds true if the mother has been vaccinated with toxoid early enough before parturition. The results of such trials have been published by Sorrentino (1931) and by Liebling and Schmitz (1943). Table I corroborates their findings.

Active immunisation was extremely satisfactory in women with some natural immunity, even if their antitoxin level was very low. The large majority of the women treated were previously entirely deficient in antibodies. In these cases the effect of immunisation was moderate, and in some cases it was weak. The antitoxin level in the newborn was usually above 0·02 unit per ml. of serum but fell rather rapidly.

The results of active immunisation of the children show that newborn infants can be immunised. The interval between the injection and the appearance of antibodies is often long in this age-group, but the antitoxin level subsequently attained does not differ from that of older children. At the age of 2 or 3 months the effect of immunisation is quite comparable to that in children aged 6–8 months, older children, and adults (table II).

The results of active immunisation so far discussed are all based on children who previously did not possess any passively transferred antibodies in their blood. In a special group the effect of toxoid injection was tested in children who possessed antibodies after active immunisation of the mother during pregnancy. The results (table III) show that a level of passively acquired antibodies of or above 0·1 unit per ml. apparently inhibited entirely the effect of injecting toxoid in the dosage used (whether sensitisation nevertheless occurred cannot be determined by the results). When the level of passively acquired antibodies was below 0·02 unit per ml. there did not appear to be any inhibition.

The fact that homologous antibodies interfere with active immunisation complicates the method of active

TABLE I—PASSIVE IMMUNISATION OF NEWBORN INFANTS BY INJECTING THE MOTHERS

Case no.	Age (yr.)	No. of injections of toxoid*	Antitoxin level (units per ml. of serum)		
			Mother		Child
			Before immunisation	At parturition	At birth
1	35	2	<0·004 >0·003	<20 >10	<20 >10
2	34	2	<0·003 >0·002	<16 >14	<14 >12·5
3	25	3	<0·0005	<1·6 >1·0	0·4
4	29	3	<0·0005	<0·8 >0·4	<1·6 >0·8
5	19	3	<0·0005	<0·8 >0·4	<0·4 >0·2
6	23	2	<0·0005	<0·8 >0·4	<0·4 >0·2
7	25	2	<0·0005	<0·8 >0·4	<0·2 >0·1
8	19	3	<0·0005	0·4	<0·4 >0·2
9	44	2	<0·0005	0·4	<0·2 >0·1
10	24	3	<0·0005	<0·4 >0·2	0·4
11	32	2	<0·0005	<0·4 >0·2	0·2
12	24	3	<0·0005	<0·4 >0·2	0·2
13	27	3	<0·0005	<0·4 >0·2	<0·2 >0·1
14	21	3	<0·0005	0·2	<0·1 >0·05
15	32	3	<0·0005	<0·2 >0·1	0·2
16	29	3	<0·0005	<0·2 >0·1	<0·2 >0·1
17	23	2	<0·0005	0·1	<0·005 >0·003
18	25	2	<0·0005	<0·1 >0·05	<0·1 >0·05
19	24	2	<0·0005	<0·1 >0·05	<0·05 >0·02
20	27	2	<0·0005	<0·05 >0·02	<0·0005
21	27	2	<0·0005	<0·02 >0·01	<0·0005
22	27	2	<0·0005	<0·005 >0·003	0·001
23	26	2	<0·0005	<0·005 >0·003	<0·0005
24	25	2	<0·0005	<0·005 >0·003	<0·0005
25	22	2	<0·0005	<0·003 >0·001	≦0·0005
26	27	2	<0·0005	0·001	0·001
27	19	2	<0·0005	<0·0005	<0·0005
Med. vals.	29	—	<0·0005	0·2	<0·2 >0·1

* Two injections (0·2 + 0·5 ml.) or three injections (0·2 + 0·5 + 0·5 ml.) of aluminium-precipitated standard diphtheria toxoid in latter half of pregnancy.

TABLE II—EFFECTS OF ACTIVE IMMUNISATION OF NON-IMMUNE PERSONS IN DIFFERENT AGE-GROUPS WITH A SINGLE INJECTION OF 1 ML. OF ALUMINIUM-PRECIPITATED STANDARD DIPHTHERIA TOXOID

Age-group	No. of persons immunised	Time of testing	Antitoxin level (units per ml. of serum)			
			<0·0005	≧0·0005 <0·02	≧0·02	Median value
Newborn	15	Before immunisation	15	0	0	<0·0005
		1 month after immunisation	8	4	3	<0·0005
		3 months after immunisation	0	6	7	=0·02
		6 months after immunisation	0	3	6	<0·05 >0·02
2–3 months	15	Before immunisation	15	0	0	<0·0005
		1 month after immunisation	0	8	7	<0·02 >0·01
		3 months after immunisation	0	5	5	=0·02
		6 months after immunisation	0	1	4	<0·05 >0·02
6–8 months	15	Before immunisation	15	0	0	<0·0005
		1 month after immunisation	1	7	7	=0·02
		3 months after immunisation	0	2	7	<0·05 >0·02
		6 months after immunisation	0	3	3	=0·02
Older children and adults	14	Before immunisation	14	0	0	<0·0005
		1 month after immunisation	1	5	8	<0·05 >0·02

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TABLE III—EFFECTS OF ACTIVE IMMUNISATION OF INFANTS ALREADY PASSIVELY IMMUNISED

Case no.	At birth	Before active immunisation*		After active immunisation*	
	Antitoxin level (u./ml. serum)	Age (mos.)	Antitoxin level (u./ml. serum)	Interval (wks.)	Antitoxin level (u./ml. serum)
2	<14 >12·5	8	<0·8 >0·4	4½	0·4
28	<0·4 >0·2	Newborn	<0·4 >0·2	4½	<0·2 >0·1†
1	<20 >10	8½	<0·2 >0·1	4½	<0·05 >0·02
4	<1·6 >0·8	4½	<0·2 >0·1	4½	<0·05 >0·02
33	<0·2 >0·1	1¼	<0·2 >0·1	4½	<0·02
29	<0·05 >0·02	Newborn	<0·05 >0·02	4½	<0·05 >0·02‡
30	<0·05 >0·02	Newborn	<0·05 >0·02	5½	<0·01 >0·005§
13	<0·2 >0·1	4½	<0·02 >0·01	5½	0·1
10	0·4	4½	<0·01 >0·005	5	0·4
8	<0·4 >0·2	5	<0·01 >0·005	4½	<0·8 >0·4
31	<0·003 >0·002	Newborn	<0·003 >0·002	4½	0·01‖
18	<0·1 >0·05	7½	0·002	7	<0·1 >0·05
6	<0·4 >0·2	7	<0·003 >0·001	4½	0·05
32	—	7½	<0·003 >0·001	5½	<0·2 >0·1
14	<0·1 >0·05	5	<0·003 >0·001	7	0·2
11	0·2	9¼	<0·002 >0·001	6	0·2
12	0·2	4½	0·001	5½	<0·1 >0·05
3	0·4	4	<0·001 >0·0005	4	<0·2 >0·1
34	>0·02	7	<0·001 >0·0005	4½	<0·1 >0·05

* With a single injection of 1 ml. of aluminium-precipitated standard diphtheria toxoid.
† 13 weeks = 0·05 ; 27 weeks <0·01 >0·005.
‡ 8 weeks <0·05 >0·02 ; 21 weeks <0·1 >0·05.
§ 13 weeks <0·02 >0·005 ; 29 weeks <0·05 >0·02.
‖ 24 weeks <0·05 >0·02.

immunisation of infants. One cannot establish active immunity until the level of passively acquired antibodies has fallen below the "protection level." This fall takes place at very different intervals from parturition until over the age of 1 year, depending on the titre originally transferred from the mother. At the age of 8 months two of the children (see table III) still presented titres as high as <0·8>0·4 and <0·2>0·1 unit per ml.

DISCUSSION

Vaccination of Infants

In countries where the natural immunity against diphtheria is low, and passive immunity in the newborn consequently rare, vaccination should preferably be carried out in the first three months of life and booster doses given at the age of 1 year and on entering school.

In countries with more or less widespread natural immunity passively transferred antibodies may interfere seriously with the effect of vaccination in the first period of life. Hence vaccination on a large scale should not be attempted in infants under the age of 6 months.

Passive immunisation of the offspring by the injection of toxoid in the mother during gestation is feasible but should be used only where there is a serious risk of epidemics of diphtheria involving the infant during the first months of life. Subsequent active immunisation should then be carried out as in naturally immunised persons.

Ability of Infants to produce Antibodies

Most workers in this field have underestimated the capacity of infants to produce antibodies. This may be explained by the following facts :

(1) The inhibitory effect of the passively transferred antibodies was not known.

(2) The delayed antibody response of newborn infants was not recognised.

(3) The results of immunisation in the infant were compared with those of the older child and the adult. Even if the latter were Schick-positive, some of them may have been under the influence of natural antigen previously, whereby the injection of toxoid had the effect of a booster dose.

(4) The non-precipitated toxoids formerly in use exerted an antigenic effect which was probably weaker, and certainly of shorter duration, than that of the precipitated toxoids used now. This is especially important in the slowly responding newborn infant.

The favourable results of immunisation against diphtheria in the first 3 months of life (Vahlquist 1946, Vahlquist et al. 1948) are comparable with the findings of Sako (1947) in vaccination against pertussis and of Rydén (1946) in B.C.G. vaccination. The old concept of a very deficient power of antibody formation during the first 6 months of life obviously requires revision.

SUMMARY

Natural antitoxic immunity against diphtheria is now low in many parts of the world. Consequently newborn infants to a great extent lack antibodies against diphtheria.

By active immunisation of a pregnant woman a passive protection may be transferred to her child.

Active immunisation of newborn infants is feasible. The production of antitoxin is often retarded in the newborn, but the titre finally achieved is satisfactory.

The presence of passive antibodies in concentrations exceeding 0·1 unit per ml. inhibits the action of antigen. Consequently active immunisation against diphtheria should be delayed until the level of passively produced antitoxin has fallen.

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GASTRIC BIOPSY

REPORT ON FIFTY-FIVE BIOPSIES USING A NEW FLEXIBLE GASTRIC BIOPSY TUBE

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WE describe here a simple and effective method of biopsy of the gastric mucosa, using a flexible tube we have designed. So far 55 specimens have been obtained and much information has been gained. There has been no evidence of pain or of hæmorrhage.

Patients with different gastric lesions were examined so that we could explore the value of the procedure. Patients who tended to bleed, such as those with cirrhosis of the liver, were not selected. The diagnoses in 48 patients were peptic ulcer (11), carcinoma of the stomach (3), chronic gastritis (12), pernicious anæmia (5), hæmochromatosis (2), and miscellaneous (12); 3 normal controls were included.

Gastric biopsy was suggested to us by Kenamore et al. (1946), who described a biopsy forceps connected to

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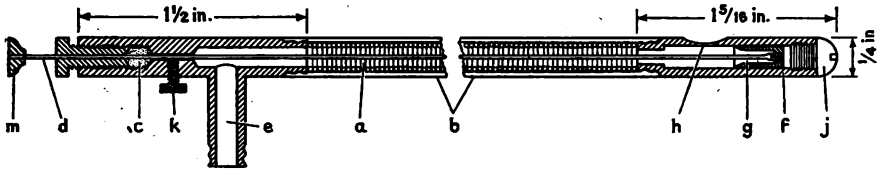

Fig. 1—Flexible gastric biopsy tube: *a*, Bowden wire casing; *b*, plastic tube; *c*, vacuum-tight gland; *d*, operating wire; *e*, lateral exhaust tube; *f*, steel cylinder; *g*, cylindrical knife; *h*, hole; *j*, terminal screw; *k*, fixation screw; *m*, handle. A knuckle of mucosa is sucked into the hole and cut with the knife.

the Schindler flexible gastroscope. We thought that it would be of value to design a simple flexible biopsy tube which could be used without the aid of a gastroscope or an X-ray screen, and which would give information about diffuse lesions of the stomach. The design of our instrument is shown in fig. 1.

The outer casing (*a*) of the Bowden wire is a close-wound spiral ($2^1/_2$ mm. outer diameter) of 28-gauge stainless steel inserted in a close-fitting plastic tube (*b*). The proximal end is fitted to a vacuum-tight gland (*c*) through which passes the inner operating wire (*d*) of 22-gauge stainless steel with handle (*m*). A lateral tube (*e*) allows connexion to a hand vacuum pump through a rubber tube. The operating wire can be fixed by a screw (*k*). The distal end is fitted to a stainless-steel cylinder (*f*) lapped to fit the knife (*g*). The knife is screwed onto the end of the operating wire which screws it up, and down past a $^3/_{32}$ in. diameter countersunk hole (*h*) drilled in the cylinder wall. The cylinder end is fitted with a removable screw (*j*) which allows the knife to be pushed out and unscrewed for obtaining the specimen, cleaning, and sharpening. The tube is about 100 cm. long. Levels I, II, and III are marked on the tube at 45, 55, and 65 cm. respectively from the lateral hole.

This describes the present model. An earlier less flexible model was used for the first half of the series. Before clinical use the instrument was tested on the bench with a fresh specimen of stomach removed at operation.

TECHNIQUE

The biopsy is usually done in the morning after the patient had been fasting for at least nine hours. Surface anæsthesia of the mouth and pharynx is obtained with 15 ml. of 3% cocaine with adrenaline 1 in 10,000. A third of this solution is applied with a de Vilbis spray, and the remainder is used for gargling. With the patient sitting, a fine stomach-tube is passed. The stomach is emptied by posturing, aided by gentle aspiration. The fasting content is measured, tested for free acid, and straightway mixed with equal parts of 95% alcohol.

The biopsy tube is passed with the patient lying on his left side, with his head flexed and resting on a pillow. The operator's left index and middle fingers are used to guide the tip over the back of the tongue. When the tip engages in the pharynx, the patient is told to swallow, and it readily passes into the upper œsophagus and rapidly into the stomach. At this juncture the patient may experience slight epigastric discomfort, which is immediately relieved by withdrawing the instrument a few centimetres. The depth is noted. If level I has not been reached, a hold-up at the cardia is probable. A few deep breaths usually overcome this obstruction. The specimen is then cut by rapidly thrusting down the handle, applying negative pressure, firmly pulling up the handle, and releasing the pressure. This action sucks in a knuckle of mucosa, which is then cut off. The specimen usually includes muscularis mucosæ, the separation taking place at the junction of muscularis mucosæ with the connective tissue of the submucosa (fig. 2). Before withdrawal the handle is depressed to release the mucosa should the cutting be incomplete. A second section may be made after withdrawing the tube a few centimetres (depending on the original depth).

The tube is next removed, and the patient is instructed to remain lying down and to spit out any saliva. The tube is inspected, to see whether a specimen has been obtained, by removing the terminal screw and forcing out the cutting cylinder. This is taken off and emptied. If no specimen is seen, the tube is blown through with the pump or a gas cylinder. This blows out mucus and any retained specimen of stomach mucosa. The specimen is immediately placed in fixing fluid. If no specimen has been obtained, the instrument may be cleaned and sterilised and the procedure repeated, or preferably a second instrument may be passed without delay.

Fig. 3—Biopsy specimen of mucosa of body of stomach in chronic gastritis (case 1), showing considerable glandular atrophy, general inflammatory infiltration, a large collection of lymphoid cells, cystic dilatation of neck portion of a gland, and fibrosis of muscularis mucosæ. (Hæmatoxylin and mucicarmine.) (× 88.)

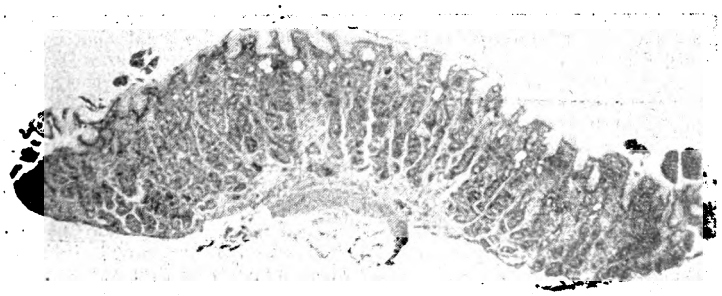

Fig. 2—Biopsy specimen of mucosa of body of normal stomach, showing extent of specimen. (× 28.)

The tube is cleaned soon after use by attaching the lower end to a filter pump and sucking through water, alcohol, and then ether. It is finally wiped over with antiseptic ('Zephiran' 1 in 100) to sterilise it. It is essential that the knife edge be sharpened after every two or three operations. Spare cutting cylinders are useful.

AFTERCARE OF PATIENT

The patient lies down for an hour. For the next two days he takes a light diet with liberal quantities of milk. Our patients have not experienced any pain when the fragment of mucosa has been cut nor any subsequent abdominal symptoms. There may be slight

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Fig. 4—Biopsy specimen of mucosa of body of stomach in chronic atrophic gastritis (case 2), showing gross glandular atrophy, one small remaining group of parietal cells, large collections of lymphocytes and fibroblasts at base of mucosa, fibrosis and thickening of muscularis mucosæ, and patchy metaplasia of surface epithelium to intestinal type. (Hæmatoxylin and mucicarmine.) (× 67.)

soreness of the throat next day. Only one patient caused anxiety.

This was a debilitated man, aged 67, with a large gastric ulcer (later proved malignant) and auricular fibrillation. He had difficulty in swallowing the tube (the older model) and probably inhaled some saliva. Later in the day he developed acute pulmonary œdema, which responded to morphine and penicillin. A subtotal gastrectomy was successfully done nine days later.

In 25 of the biopsies a gastroscopy was performed within five minutes of completing the biopsy. No evidence of trauma or hæmorrhage was observed, except about 1 ml. of blood in one patient and a small hæmatoma 1 cm. in diameter in another. In 7 patients partial gastrectomy was done within seven days of biopsy. No evidence of recent trauma was observed in the portion from which the biopsy specimen had been taken.

Biopsy was performed on 32 outpatients, who were allowed to go home after resting for two hours. None showed ill effects.

FIXATION AND STAINING OF BIOPSY SPECIMENS

The material was fixed in 10% formol saline, dehydrated, and embedded in paraffin according to standard technique for small pieces of tissue. The routine stain was hæmatoxylin and eosin. Mucin was stained with Mayer's mucicarmine, collagen with van Gieson's picric acid and acid fuchsin, and reticulum by Gomori's silver impregnation method. Pepsinogen granules within chief cells were stained in the formalin-fixed material by a modification of the method of Bowie and Vineberg (1935). The treated gastric contents were centrifuged, and a smear of the sediment was stained according to the technique of Papanicolaou and Traut (1943), which enabled us to compare the cellular nature of any exudate present with the histological changes in the mucosa.

The gastrectomy specimens were examined by the "Swiss roll" technique of Magnus (1937), whereby the entire length of the resected portion could be examined histologically and compared with the previous biopsy sample.

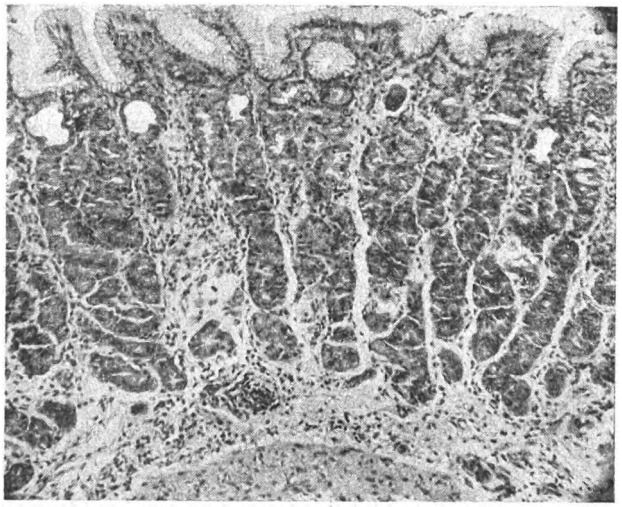

Fig. 5—Biopsy specimen of mucosa from body of normal stomach. (× 84.)

ILLUSTRATIVE CASE-RECORDS

Case 1.—A male, aged 45, with only minor flatulent dyspepsia. His diet was satisfactory and he was temperate. Barium meal: the stomach and duodenum were within normal limits, but the stomach was angulated with "cup and spill" contour. Test-meal: achlorhydria to a gruel meal but a moderate flow of free acid to both histamine and insulin. Gastric biopsy: tube passed into the upper third of the stomach, where it engaged in the "cup" (later confirmed by radiography). There was no distress when the biopsy specimen was cut. Histology: chronic gastritis (fig. 3). The fasting gastric contents stained by Papanicolaou method showed profuse polymorphs. The saliva contained scanty polymorphs.

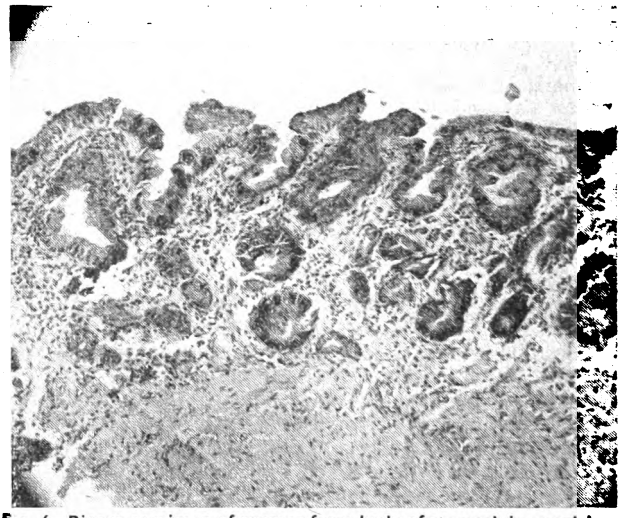

Fig. 6—Biopsy specimen of mucosa from body of stomach in pernicious anæmia (case 3), showing glandular atrophy, complete disappearance of chief and parietal cells, thickening and fibrosis of muscularis mucosæ, and metaplasia of surface epithelium with formation of mucous goblet cells. (Hæmatoxylin and mucicarmine.) (×84.)

This patient had mild flatulent dyspepsia. Stomach biopsy showed that the "cup" of the "cup and spill" stomach was the site of chronic gastritis.

Case 2.—A female, aged 56, with twenty years' history of flatulent dyspepsia and occasional vomiting. Five years after the onset she had been seriously ill for fourteen days with "food-poisoning." Her diet had been satisfactory and she took no alcohol. During the two years she was under observation in the outpatient department of the Royal Melbourne Hospital she constantly complained of flatulent dyspepsia with epigastric discomfort. There was no relief with acid, alkali, or sedative. Examination always showed diffuse tenderness in the epigastrium. Barium meal: stomach and duodenum within normal limits. Gastroscopy: suggestive of atrophic gastritis. Test-meal: histamine-fast achlorhydria with excess mucus. Hæmatological examination normal. Gastric biopsy was done without untoward incident. Histology: gross chronic atrophic gastritis (fig. 4).

The history and special investigations suggested chronic atrophic gastritis. This was confirmed by gastric biopsy.

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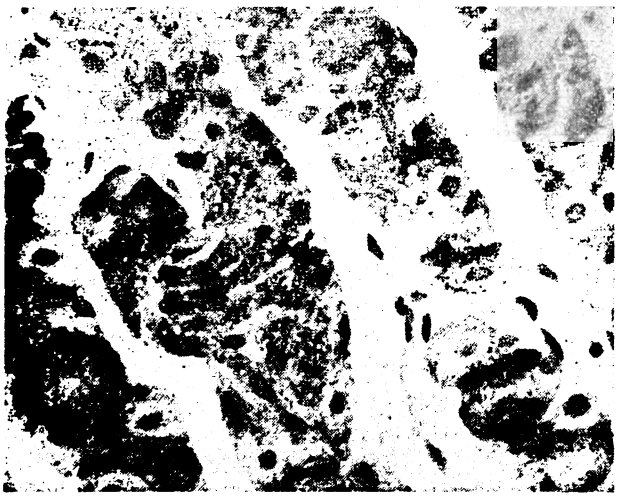

Fig. 7—Biopsy specimen of stomach in hæmochromatosis and achlorhydria (case 4), showing granules of hæmosiderin packing chief cells and occurring more sparsely in parietal cells of gastric glands. (Prussian blue.) (×422.)

Case 3.—A male, aged 73, was admitted to the Royal Melbourne Hospital with pernicious anæmia (Hb 5·4 g.), and early subacute combined degeneration of the cord. Test-meal: histamine-fast achlorhydria. Barium meal: stomach and duodenum within normal limits. Gastroscopy: atrophic gastritis. The patient showed an optimal response to liver therapy. Gastric biopsy was done without untoward incident. Histology: typical atrophic mucosa of pernicious anæmia (fig. 6).

Gastric biopsy in a patient with treated pernicious anæmia revealed typical atrophic gastritis. A normal control (fig. 5) has been included for comparison.

Case 4.—A female, aged 63, was admitted to the Royal Melbourne Hospital with forty years' history of attacks of abdominal pain, nausea, and anorexia, unrelieved by alkali or acid. During the past two years there had been increasing weakness. Examination revealed the typical appearance of hæmochromatosis. The liver was enlarged and firm. The tip of the spleen was palpable and firm. Hippuric-acid excretion was impaired. Liver biopsy showed typical hæmochromatosis with considerable fibrosis. There was no glycosuria, but the glucose-tolerance curve was that of mild diabetes. Skin biopsy: a little hæmosiderin in the epithelium of the sweat glands. Test-meal: histamine-fast achlorhydria and lowered pepsin secretion. Barium meal: within normal limits. Gastric biopsy was done without causing distress. Histology: the mucosa was of normal depth. Hæmosiderin was present in parietal cells and chief cells, particularly the latter (fig. 7). The chief cells had a very scanty pepsinogen content.

It is tempting to suggest that in this case of hæmochromatosis the deposition of hæmosiderin in the chief and parietal cells of the gastric mucosa impaired their function.

DISCUSSION

At present most of our knowledge of the histopathology of the stomach is based on necropsy specimens (in which special precautions are needed to reduce post-mortem changes) or on operation specimens. In the former the histological picture may be affected by the cause of death; in operation specimens ulcer and carcinoma form the bulk of the cases; and in both kinds of specimens no serial observations are possible. The technique described here is simple, does not distress the patient, and is almost free from complication, and the specimen is adequate.

The present 55 biopsy specimens were obtained in 83 attempts. Biopsy has been attempted on several of the 48 patients in the series more than once; and 2 specimens have been obtained from each of 5 patients. Failure to obtain a specimen (28 out of 83 attempts) depends on factors as yet unknown.

In clinical practice biopsy may establish a histological diagnosis when there is a diffuse lesion of the stomach. This is exemplified in cases 1 and 2. The method will also be an adjunct to clinical and pathological study in many diseases in which the gastric lesion is not necessarily the chief feature. This is shown in cases 3 and 4. The method lacks any "siting." It therefore has no rôle in the differential diagnosis of localised lesions, such as ulcer and carcinoma. The depth at which the biopsy is done and the histology of the specimen give much information about the level of the stomach from which the piece is obtained. Gastroscopy subsequent to the biopsy has not been of value in this problem. Some barium studies have been made and are informative.

SUMMARY

A flexible gastric biopsy tube is described.

With this instrument specimens of gastric mucosa suitable for histological study have been obtained in 55 cases, without causing hæmorrhage or pain.

The value of the method and its limitations are discussed.

We wish to thank the honorary medical staff of the Royal Melbourne Hospital for providing clinical material. We deeply appreciate the help of those members of the resident medical staff and students of the hospital who acted as controls. The photomicrographs were prepared by Mr. H. Matthaei, of the University of Melbourne.

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PRELIMINARY TRIALS OF BISTRIMETHYLAMMONIUM DECANE AND PENTANE DIIODIDE (C10 AND C5) IN MAN

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THE clinical use of members of the polymethylene bistrimethylammonium series as agents for neuromuscular and for ganglionic block has been suggested on the basis of animal experiments (Paton and Zaimis 1948). In the following trials the decane and pentane diiodide have been used (C10 and C5 respectively). The salient features of their pharmacological actions may be summarised as follows:

(1) C10 injected in small doses into a cat or other animal causes a neuromuscular block which spares the respiratory muscles; it is not antagonised by anticholinesterases, but a useful antidote exists, if needed, in C5 (which is virtually devoid of curarising activity). C10 has much less activity in liberating histamine or heparin (MacIntosh 1948) and has less activity in paralysing autonomic ganglia than has an equal weight of *d*-tubocurarine chloride.

(2) C5 is powerful in paralysing autonomic ganglia in cat and rabbit—as shown by block of the superior cervical ganglion, fall of blood-pressure, paralysis of the peristaltic reflex of the small intestine, and paralysis of the action of the vagus on the heart. C5 is thus similar to tetraethylammonium iodide, but it is 10–20 times more active, and its effects last two or three times as long. C5 was used for convenience in these trials, although C6 (the hexane derivative) was originally proposed. The two drugs act alike, C5 being slightly more potent as an antidote to C10, and C6 being slightly more active in paralysing autonomic ganglia.

With C10 in particular there is great variation of potency with the species of animal used for the tests.

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We describe here preliminary trials of C10 and C5 to ascertain the sensitivity of man to these drugs and to find whether their effects in man differ from those in other animals. This is a first step towards assessing their clinical value.

EFFECTS OF C10

Tests have been made on three volunteers (W. D. M. P., E. J. Z., and G. O.) on five occasions, on two of which C5 was also administered. C10 3 mg. was slowly injected intravenously in 50–90 sec. In each trial the first effect noticed subjectively was on the eyes and eyelids, within 20 sec. of the beginning of the injection. Paralysis reached a maximum in about 4 min., recovery beginning in about 10 min. and being complete in 1 or 2 hours.

Paralysis began in the eyelids, ocular muscles, and facial muscles, and later affected the neck, trunk, and limbs. The degree of paralysis varied within limits among the subjects; at the peak of the paralysis two of them were incapable of moving their limbs or head at all, and had virtually complete paralysis of hand strength (figs. 1 and 2); the third was very considerably weakened, and his hand strength fell by about 60%. In all cases there was a considerable reduction in abdominal tone and in the power of contracting the abdominal muscles. The respiration, however, was not embarrassed, though the vital capacity was diminished at the peak of the paralysis by about 35%. Speech was impaired, the voice becoming weaker and lower in pitch, but coughing was always possible; swallowing was weakened but never disappeared. The jaw muscles were relaxed, but there was no consequent obstruction to the respiration. The degree of paralysis was roughly comparable with that obtained in a conscious subject with 15–20 mg. of *d*-tubocurarine chloride.

Side-effects.—No important side-effects were seen. There was a rise of pulse-rate and blood-pressure,

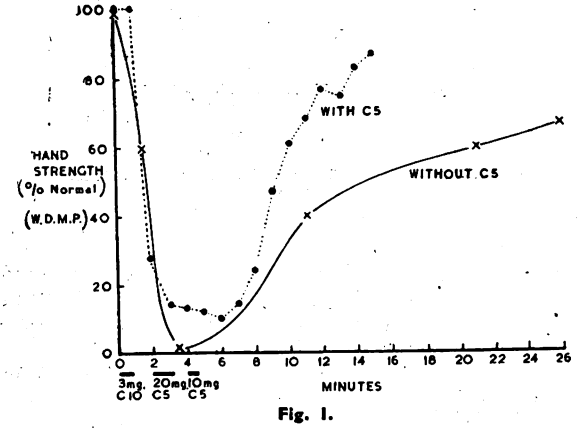

Fig. 1.

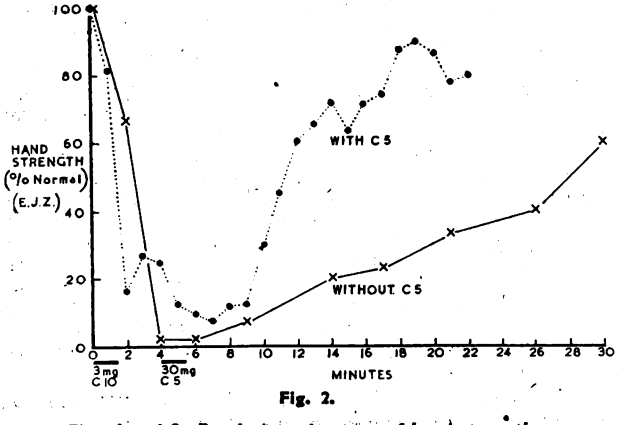

Fig. 2.

Figs. 1 and 2—Paralysis and return of hand strength.

DURATION OF PARALYSIS IN MINUTES

Power recovered	Volunteer			
	E. J. Z.		W. D. M. P.	
	C10 alone	C10 with C5	C10 alone	C10 with C5
Leg-lifting	17	8	11	9
50% hand strength	28	11	15	9
Abdominal tone ..	20	9	20	11
Ocular muscles ..	15	8	30	9
Ability to stand up..	45	26	45	20

synchronous with the development of the paralysis, which began to pass off in 5 or 6 min. (probably this was of emotional origin). Electrocardiograms taken before, during, and after the paralysis were normal in every trial. Examination of the capillaries of the finger-nail bed in one subject showed a vasoconstriction starting 14 sec. after the injection, reaching a peak at 100 sec., and then returning to normal; there was no evidence of vasodilatation. Salivation was not more, but possibly less, than normal. During the beginning of the paralysis a vague feeling of slight tightness of the muscles was noted subjectively for a brief time and then passed off. C10 also appeared to have a slight narcotic action, but it was difficult to dissociate this subjectively from the effects of an almost complete motor paralysis. Sensation was normal.

The accompanying table shows the duration of paralysis in the various muscles. It must be noted, however, that it is difficult to estimate muscle strength in man quantitatively, and these times are necessarily only approximate. On the whole, the time-scale of the paralysis was similar to that of one of equivalent maximum depth due to *d*-tubocurarine chloride, except that the ocular effects do not appear to last so long.

Antagonist.—Observations on the effects of C5 alone are described below. Doses of 30 mg. given at the peak of a paralysis due to C10 substantially accelerated recovery. The first subjective sign was a sense of ease of respiration. Figs. 1 and 2 show the extent to which C5 accelerated recovery of hand strength, and the table shows the same for other muscular functions. There was no fall in blood-pressure, though there was detectable flushing of the skin of face and hands and slight conjunctival suffusion. Electrocardiograms were normal throughout, and there were no other side-effects.

EFFECTS OF C5

C5 has been administered to three normal subjects (W. D. M. P., E. J. Z., and F. E. C.) in doses of 20–40 mg. intravenously. This did not change the blood-pressure while the persons were supine, but there was detectable flushing and warming of face and hands, together with a feeling of warmth in these places, and some conjunctival suffusion. No other effects were noticed. When the subjects stood up, however, the systolic pressure fell by 20–35 mm. and the diastolic by 5–15 mm.; in one person this fall led to a severe syncopal attack. When the subjects lay down again the blood-pressure returned to normal. Such falls in blood-pressure were obtainable by assuming the erect posture as late as 30 min. after the injection. Electrocardiograms taken during the tests were unchanged throughout.

DISCUSSION

The results show that man is very sensitive to C10, and that in this he resembles the cat rather than the monkey, rabbit, mouse, or rat. The doses of C10

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required for paralysis in cat and man are almost identical We have not made direct comparisons between C10 and *d*-tubocurarine chloride as regards their respiratory actions in man, but a comparison of the descriptions of respiratory depression by *d*-tubocurarine chloride (Prescott et al. 1946; Hobson and Prescott 1947) with the results of these trials indicates that the relative sparing of respiration by C10 in the cat is found in man too. Similarly, the dose of C5 required to produce vascular effects (about 0·5 mg. per kg. of body-weight) is the same in man as in the cat, and in both species can also be seen the greater potency and longer duration of action of C5 compared with tetraethylammonium iodide. It is therefore probable that man will resemble the cat in the absence of side reactions with C10, and in his other responses to C5. The high potency of these drugs and the absence hitherto of undesirable side-effects increase the prospects of their clinical usefulness in those fields where *d*-tubocurarine chloride and tetraethylammonium iodide are of service. Full clinical trials are being undertaken under the sponsorship of the Medical Research Council, and the results will be reported later.

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Reviews of Books

Headache and Other Head Pain

HAROLD G. WOLFF, professor of medicine (neurology) and associate professor of psychiatry, Cornell University. London: Oxford University Press. 1948. Pp. 642. 63*s*.

DURING the last fifteen years Prof. Harold Wolff and his associates have made a series of intensive studies of pain in general and headache in particular. These studies are now gathered together in this volume, which also includes an extensive review of previous work and will appeal to all serious workers in this field. For those with a general interest in the subject—and since headache is one of the commonest symptoms this includes the majority of clinicians—Professor Wolff summarises the conclusions and indicates the clinical features of headache arising from different sources and different maladies.

With Dr. Bronson Ray, his neurosurgical colleague, he has made an exhaustive investigation of pain-sensitive structures in the cranial cavity, confirming and extending the observations begun by Lennander. He postulates six basic mechanisms for headache arising within the cranial cavity: (1) traction on the veins that pass to the venous sinuses from the surface of the brain, and displacement of the great venous sinuses; (2) traction on the middle meningeal arteries; (3) traction on the large arteries at the base of the brain and their main branches; (4) distension and dilatation of intracranial arteries; (5) inflammation in or about any of the pain-sensitive structures of the head; and (6) direct pressure by tumours or adjacent tissue on those cranial and cervical nerves which contain many pain-afferent fibres from the head. The sensibility of intracranial structures, and the distribution of pain arising from them, are examined.

The reader unfamiliar with the subject will not find that the work leaves him with a clear conception of the mechanism of headache: there are still too many obscurities in the subject. At least it is clear that the old hypothesis of headache due to raised intracranial pressure is dead—or rather should be if medical men in general were impressed by evidence. In meningitis the fundamental process seems to be a raising of the sensibility of the pain-sensitive areas in the meninges, to which mechanical distension may add its own component. In tumour distortion of intracranial structures or direct pressure by the tumour on sensitive areas seems to be the responsible stimulus. The contribution made by contraction of the extracranial muscles deserves study. Early in the book Professor Wolff accepts the muscular contractures that accompany meningitis (neck rigidity, Kernig's and Brudzinski's signs) as being due to involvement of the sensory roots in the inflammatory process; but it seems more probable that these are really the reflex contractions which accompany a deep sensory nerve-ending stimulation, comparable to those found in pleurisy, peritonitis, and arthritis. Later he points out that electromyography shows increased muscular contraction in histamine headache, as well as in eyestrain and in stimulation of the paranasal sinuses and other extracranial structures. Whether these contractions add a component to the pain is difficult to judge. Dr. Wolff thinks they do—sometimes a major component—and he backs his argument by the effects of local anæsthesia in the case of pain induced from the teeth. But though electromyography shows that muscles are contracted, it does not prove this contraction to be a source of pain. Many years ago Ryle pointed out that in peptic ulcer contraction of the rectus abdominis persists long after the pain has gone.

By bringing questions of this sort, as well as the solid progress achieved, to the notice of others Dr. Wolff has rendered a great service to his subject.

Malignant Disease and its Treatment by Radium

(2nd ed.) Vol. I. Sir STANFORD CADE, K.B.E., C.B., F.R.C.S., M.R.C.P., surgeon, Westminster Hospital, Mount Vernon Hospital and Radium Institute. Bristol: J. Wright. 1948. Pp. 383. 52*s*. 6*d*.

THE first edition of this book was destroyed by bombing almost as soon as it was published in 1940, and it has been known chiefly as a coveted possession on other people's shelves. The second edition will be in four volumes, of which this, the first, deals with the fundamentals of cancer, and its treatment by radium, covering such subjects as the action of radiation on normal and tumour tissues. There is a new chapter, by Dr. F. G. Spear, on tissue culture and experimental radiology, but on the whole only minor changes have been needed to bring the text up to date. When a book contains the elements of physics and radiopathology and is intended for use by clinicians, it is perhaps unreasonable to complain that radiobiology has not been reconsidered in the light of the more recent work in genetics, biochemistry, and viruses. The present edition closely follows the original, preserving its characteristics as a pioneer textbook in its historical approach, encyclopædic references, and impressive record of personal observation. In deciding to issue the new edition in four volumes the publishers have taken advantage of the author's command of a huge mass of material, while attending, at the same time, to the reader's convenience.

Hypnotherapy

A Survey of the Literature. MARGARET BRENMAN, PH.D., professor of psychology, Menninger Foundation center of the department of psychology, University of Kansas; MERTON M. GILL, M.D., associate psychiatrist and assistant director of the department of research of the foundation. London: Pushkin Press. 1948. Pp. 271. 18*s*.

IN the 1914-18 war the amnesias, paralyses, and other recent hysterial states associated with war neuroses were often treated by hypnotic suggestion. In 1939–45 not only was gross "conversion" hysteria rather less common but techniques such as narco-analysis, which are less exacting for the physician, largely took its place. Today there are signs of a revival of hypnosis both as a method of direct treatment by suggestion and as a means of shortening the investigative period of psychotherapy. In this field the workers at the Menninger clinic have been prominent, and many who served as psychiatrists in the Forces will remember the review of hypnotherapy by Professor Brenman and Dr. Gill which was circulated to them by the Josiah Macy Foundation. The first part of the present book is a reprint of that review: it traces the progress of thought in relation to hypnotism in the last fifty years, and also provides a first-class bibliography. The second part consists of four case-histories, illustrating the use of hypnosis in treatment. In these cases the tendency

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to interpret symptoms in terms of current psychoanalytic theory, rather than to allow the patient some initiative in working out the dynamics of his symptoms, is in contrast to the eclectic attitude to psychopathology shown in the main review. The final section is devoted to an experimental study of hypnosis, of limited interest to readers seeking knowledge of therapeutic procedures.

Feeding the Human Family

Science Plans for the World Larder. F. LE GROS CLARK, M.A. London: Sigma Books. 1948. Pp. 125. 7*s.* 6*d.*

IN this remarkable book Mr. Le Gros Clark reviews the food eaten by mankind, its origins and its deficiencies. A wealth of information, ranging from farming methods to medical problems, is presented with essential accuracy and yet so simply and readably that it can be absorbed by anyone from the sixth form onwards. Equally the specialist in these fields will find many unexpected and thought-provoking ideas.

One of the issues discussed is that of the disposal of agricultural surpluses. The work of Orr and MacDougall in preaching expansion of food-production to the level required by human needs is well described; and the birth of the Food and Agriculture Organisation of the United Nations, in which both of these men have played their part, is explained as an important advance, though its present activities are criticised as lacking force. Unfortunately hardly anything is said about food-production in Soviet Russia, which has refused to join F.A.O.

The book is well produced, with stimulating chapter headings, instructive maps and charts, some good representative photographs, and an appendix of statistics. Particularly interesting from a medical standpoint is an ingenious table relating infant-mortality rates and the expectation of life to the percentage contribution of cereals and potatoes to the diet in various countries.

Human Ancestry

R. RUGGLES GATES, F.R.S., emeritus professor of botany in the University of London; research fellow in biology, Harvard University. Harvard, Mass.: Harvard University Press. London: Oxford University Press. 1948. Pp. 422. 42*s.*

As in his *Human Genetics*, Professor Gates has brought into accessible form a large and scattered literature. Physical anthropologists and human biologists—the latter term is beginning to subsume the former—have solid cause for satisfaction in the comprehensiveness of his industry. For example, in the chapters on South and East Africa we have for the first time full documentation of extensive work which has had too little attention.

Less general approval will be given to the author's claim that the main types of living man should be ranked as species. Though faint-hearted readers may find themselves borne down by the argument, the fact remains that some of the palæontological evidence adduced can be otherwise interpreted. Thus much is built on the belief that Africanthropus produced "Boskop" man, who later developed into the modern Bushman and Hottentot and by specialisation into the African Negro as well; but the present status of Africanthropus, morphological or geological, is about as reliable as the tentative reconstruction of the exceptionally fragmentary skull remains (p. 99). Similarly Sinanthropus is offered as the first Mongolian, and it does not particularly disturb Professor Gates that some of the alleged specific Mongolian features, such as the torus palatinus, are also common among Melanesians and Australians. On similar reasoning, why should not the Cape Bushmen claim species affinity with the Neanderthalers of Europe in the common possession of taurodontism?

About the local differentiation of human varieties there is of course wide agreement among anthropologists; and manifestly there has also been continental or regional evolution within the Hominidæ. Professor Gates invites us to believe that the differences amount to species formation and that the dissimilarities between modern groups of man are more impressive than the resemblances. Some of the resemblances he would dismiss as manifestations of parallelism and parallel mutation, and this may be the correct explanation of sporadic resemblances between distant communities such as the occurrence of the A blood-group among a few Indian tribes or the Mongoloid characters of some Bushmen. But in this thesis parallelism is invoked to explain the totality of resemblances. It is interesting therefore that, though the postulated and distinctive "species-ancestors" are conspicuous for their endocranial differences, Professor Gates has not found in his separately evolved human species any brain differences to match such contrasting characters as those of hair form or skin colour. In their cerebral processes, no less than in their mating and reproductive behaviour, his species of men exhibit a degree of identity not easily explained by convergence. The idea of parallelism has to be worked very hard.

Elementary Atlas of Cardiography (Bristol: J. Wright. 1948. Pp. 108. 12*s.* 6*d.*).—In this little book Dr. H. Wallace Jones, Dr. E. Noble Chamberlain, and Dr. E. L. Rubin present 57 figures depicting the commonest cardiographic changes. These are clear for the most part and give the medical student as much as he needs to know; but a few might be improved on. The second part of the book deals with the radiographic appearances of the heart and great vessels, and shows, in an excellent series of pictures, some common conditions which produce a characteristic configuration.

Recent Advances in Obstetrics and Gynæcology (7th ed. London: J. & A. Churchill. 1948. Pp. 326. 21*s.*).—Seven editions in 20 years, of which three (and a reprint) have appeared within the last 5, testify to the editorial energy of Mr. Aleck Bourne and Mr. Leslie H. Williams. Their contributors have supplied no fewer than six new chapters to replace a similar number displaced. An outstanding opening chapter on diet in pregnancy occupies 36 pages, and deserves close study: the book is worth purchasing for this chapter alone. Recent work on the nature of lactation and the factors influencing it is discussed, and among the new chapters is one on the anæmias of pregnancy by Prof. L. J. Davis. Chapters on carcinoma of the cervix, on stress incontinence of urine, on sympathectomy, on penicillin, and on radiology and radiotherapy are all good, though that on radiology is perhaps somewhat overweight. The whole work is of a very high standard.

The Care of Tuberculosis in the Home (2nd ed. London: Hodder & Stoughton. 1948. Pp. 112. 7*s.* 6*d.*).—The great strain now being placed on the tuberculosis services of the country, owing to lack of nursing staff and therefore of beds, has forced authorities to arrange for treatment of many patients in their own homes—at least for some months, until a vacancy in a sanatorium is secured. This can only be done with the full coöperation of the patient and his relations. This book by Dr. James Maxwell has been designed primarily for the intelligent patient, and sets out to explain the essential facts of the disease and the mode of treatment. It is written in simple language and to the point, and stresses not only what can be done but also what cannot be done. It will also be found helpful by those doctors, increasing in number, who think it wise to take the patient into their confidence and who view the management of tuberculosis as team-work.

Short History of Ophthalmology (2nd ed. London: Staples Press. 1948. Pp. 103. 8*s.* 6*d.*).—Prof. Arnold Sorsby traces the history of ophthalmology from its origins in ancient Greece to modern times, giving the reader a good general outline of the development of spectacles and the ophthalmoscope, the different conceptions of glaucoma and cataract, how the anatomy and physiology of the eye was depicted by the ancients, and how therapeutics have changed through the years. The ophthalmoscope was first received with scepticism. It was thought that the interior of the eye could not be illuminated; but when that proved false and Helmholtz devised his "eye mirror" many said that so much light inside the eye would be injurious, and would in fact cause those very ills which ophthalmologists sought to cure, while some even gave their opinion that it was a useful instrument for those oculists who had not good sight. The final chapter is a review of British ophthalmology, and the whole of the short volume is very readable.

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References:—Shortage of space precludes list of references, but full documentation may be obtained on application to Medical Dept. 41.B.

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THE LANCET
LONDON: SATURDAY, JAN. 1, 1949

Postoperative Period

THE biggest operation ever known in medicine was performed on July 5. It was an attempt to bring the many separate medical services of this country into a single integrated system which should eventually meet all needs. Like other major operations it has had some alarming immediate results: but its ultimate consequences cannot be foretold thus early. If so disposed, we can admire the skill and nerve of the surgeon and his assistants, who have achieved a technical feat probably impossible in any other large country. We can admire also the way in which the vital services have been kept going, under difficulties, by a great many people who always disapproved of the scheme and are now suffering through it. But certainly the day has not yet come for apportioning blame. In so vast an operation mistakes were inevitable, and many of them can still be rectified. Surgeons have learnt that success or failure commonly depends on their conduct of the dangerous postoperative period—on the correct interpretation of symptoms, on the management of complications, and on secondary intervention if required. The benefits of reconstructive surgery may not be apparent for a long time, and meanwhile there is often pain and disfigurement.

At the moment the most disquieting symptoms come from general practice, which seems likely to deteriorate unless remedial action is taken. In the first place, general practitioners are depressed because, unlike most other sections of the community, many of them have been obliged to do more work for less pay. The National Health Service was not of course designed for the purpose of increasing the prosperity of doctors; but the fact remains that the first Spens report, accepted in principle by the Government, envisaged an improvement in the financial status of a large proportion of general practitioners in relation to that of other professional men and women. How far the Spens Committee's recommendations are fulfilled by the remuneration now in force is partly a matter of ascertainable fact, on which comment must be withheld until the current investigation is complete. But it is also partly a matter of opinion; for the committee reported in terms of 1939 incomes and left others to decide how these should be brought up to date—having "regard not only to estimates of the change in the value of money but to the increases which have in fact taken place since 1939 in incomes in other professions." In the absence of evidence to the contrary, the opinion of ordinary people must be that if the Government persist in regarding 20% as a sufficient betterment figure for net incomes the actual effect of the recommendations, in 1949, will be to lower the relative status of the general practitioner rather than raise it, and that their virtue will thereby be nullified. Admittedly there are doctors in urban areas whose financial position has improved in the past six months; but unfortunately the benefit has generally been greatest in the type of practice that is medically least satisfactory. If this is so, it is a serious defect in the scheme, and one moreover for which the profession itself must accept some of the responsibility. Its motives have been excellent; but by opposing any substantial basic salary, and by insisting that even the £300 a year should be reserved for exceptional cases, it has removed some of the means whereby the capitation system might have been tempered to the small practice shorn of its well-to-do private patients. Capitation, uncompensated, means that the criterion of a man's worth is the length of his list; and few doctors can still earn their former incomes unless they have a long one. This is regrettable because, with the present demand for medical attention, a long list is virtually incompatible with the kind of family care which the service was supposed to promote.

But was it? Or rather, how far was the promotion of sound general practice a principal aim? The question must be asked because there are evidently two schools of thought. The first holds that under modern conditions medicine dwells in the hospitals, where alone accurate diagnosis and scientific treatment of major illness is possible. According to this school the emphasis of the new service should be on hospital and specialist services, which will deal with all the illness that matters, and the rôle of the general practitioner is chiefly to feed the hospitals. The second school, on the other hand, regard the investigation and treatment of major illness as secondary to the enormous task of relieving the troubles of everyday life, and of helping people to pursue health: the heart of medicine, they feel, is in general practice, and it is at least as important to have really good general practitioners, bringing medicine to the home, as it is to provide pleasures and palaces for patients who qualify for institutional care. Polemics apart, all will agree that the two parts of clinical medicine are complementary, and that what we have to do is to strike a suitable balance between them; but there certainly seem to be special reasons at present why the hospital school should not be in the ascendant. Hospital beds, fully staffed, are scarce; they are becoming very expensive; and the only hope of maintaining and raising hospital standards lies in avoidance of waste. We therefore need a policy of hospital devolution: nobody should be admitted for investigation if he can be investigated equally well in an improved outpatient department, and nobody should occupy an ordinary hospital bed after he has become fit to be moved to some less elaborate, ancillary, institution—a convalescent home, a reablement centre, or a hostel for old people—or to his own home. Given suitable help, a great many patients are better at home or in some simple form of establishment, and we shall be wasting our money if we spend too much of it on hospital beds and too little on enabling the local authority and the local doctor to do their proper work. To offset the present trend towards the hospital it might, for instance, be well to supplement the practitioner's capitation fees by emoluments for socially desirable activities such as the regular care of an aged person or invalid (perhaps on behalf of the institution that would otherwise have to admit

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the case), and also for seeing patients in consultation with a specialist. Any suggestion that practitioners should be persuaded to do more rather than less work may seem unrealistic; but in the long run there can be no salvation for general practice except through restoring its medical responsibilities. Potentially, the Act has done great good, both to the public and to the profession, by removing the money barrier between patient and doctor; but it will undo this good if it thereby lowers the quality of the doctor's care. Up to date, the Government have given the practitioner a heavier and more clerical job without giving him even a hope of the new tools he was promised for it; and his present tribulations, no less than the policy of hospital devolution, demand the rapid development—if necessary, the improvisation—of health centres, which in towns offer the best chance of averting the degradation of practice under the strain now imposed. By providing him with the right environment and facilities and aids, the practitioner must be enabled and encouraged to go on practising medicine, for which more than ever he now lacks time and incentive. If his work is deprived of its medical interest and ceases to be a highly skilled occupation, regarded and remunerated as such, it will soon cease to attract any man of parts. The potential benefits of the National Health Service cannot be realised unless the overworked practitioners of today receive increasing reinforcements; and, as the Spens Committee said, "it would be disastrous to the profession and to the public if general practice were recruited only from the less able young doctors." Whatever triumphs might be scored in the hospitals, the public would then have lost rather than gained by the great operation of 1948.

Outside general practice there are other complaints against the new régime—as witness our articles on The Act in Action. For example, the relatively large payments made to dentists, ophthalmic surgeons, and opticians have annoyed everyone except the recipients. The service has, so far, disappointed a large body of trainee specialists who relied on it to find them work at once. Too much time is being spent by too many people in committees, which are apt to pay too much attention to details that should be left to their officers. And the old and baneful division of interests between voluntary and municipal hospitals shows signs of reviving here and there in a failure of coöperation between the boards of teaching hospitals and those of the regions. Nevertheless, most of these disorders are curable, and, outside general practice, the New Year finds us with many reasons for thankfulness and hope. The transfer of the hospitals to new management has been accomplished smoothly: a great number of valuable people have been enlisted in their administration; and the Minister of Health has genuinely delegated to these volunteers much of the power he acquired under the Act. The regional boards have been allowed to develop individualities and methods of their own; the English hospital tradition has been given new life and scope; and the medical profession possesses the opportunities of influence for which it asked. These opportunities extend throughout the service, and the profession, if it sets its face towards the future instead of dwelling on an irrevocable past, can help to overcome many of the difficulties that have arisen. Provided our country can continue its economic recovery, most of these difficulties can undoubtedly be surmounted; and 1949 is likely to restore confidence in a great project which the public clearly wishes to continue.

The operation was enormous and complex, and there will long be cause for anxiety. Yet after six months it is probably fair to say that the service is going on as well as could reasonably be expected—and in some respects rather better.

Intravenous Iron

EIGHTEEN months ago NISSIM [1] announced that he had prepared a solution of iron hydroxide that could safely be given by intravenous injection. The reasons why such a preparation is useful [2] are worth recapitulating. Man excretes a very small amount of iron each day, mainly through the bile. If the iron in the food is insufficient, or if it is not absorbed, the body's stores are slowly depleted and anæmia appears. The iron reserve may also be exhausted by loss through hæmorrhage, as in hookworm infestation. Where there is deficiency the iron in the enzymes cytochrome and catalase, and in myohæmoglobin, is retained at the expense of the iron in the hæmoglobin of the red cells, in the labile tissue stores (mainly in the liver), and in the plasma. In most patients the deficiency can be made good with small repeated doses of ferrous sulphate by mouth, but even under ideal conditions the daily rise of hæmoglobin will not exceed about 0·55 g. per 100 ml. blood. In many cases conditions are not ideal and the rise in hæmoglobin is insufficient or even absent. The mechanism by which iron is absorbed—chiefly from the stomach and duodenum—is curiously limited [3]: in the mucosa it combines with a protein acceptor (apoferritin) to form a compound (ferritin) that is capable of releasing it to the plasma when the plasma iron falls below the physiological level. In the plasma the iron is bound up with globulin, after which it cannot be released to unsaturated apoferritin. With large doses of iron this ferritin mechanism can be saturated in 1–2 hours, but desaturation takes days; so the rate at which iron can be transferred from the gastro-intestinal tract to the plasma is restricted. Whether defects in this acceptor mechanism account for refractoriness to iron by mouth we do not yet know.

Most of these facts (except those about ferritin) have been obtained by the use of radioactive ron tracers. The results, lately summarised by HAHN,[4] all make it clear that if we are to get enough iron into patients who have exhausted their labile stores, or cannot tolerate its administrat on by mouth, or are refractory to such administration, our only course is to give it parenterally; and so far only the intravenous route has proved practicable. NISSIM's original preparation was made from the saccharated iron of the *B.P.* This is a variable compound of uncertain composition, and when a solution is autoclaved it more often precipitates than remains clear. In our present issue Dr. SLACK and Dr. WILKINSON describe how they selected and prepared a stable iron-sucrose solution that can be safely autoclaved;

1. Nissim, J. A. *Lancet*, 1947, ii, 49.
2. Leading article, *Ibid*, p. 59.
3. Granick, S. *Chem. Rev.* 1946, **38**, 379.
4. Hahn, P. F. Advances in Biological and Medical Physics. 1948; vol. 1, p. 287.

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a very similar solution is marketed under the name 'Ferrivenin.' They agreed with CAPPELL [5] and NISSIM that a saccharated iron was most likely to be successful because, when mixed in vitro with human serum, saccharated iron and iron di-ammonium chelidamate, alone of the many compounds tested, gave no flocculation, cloudiness, or gel formation; and trial by injection into patients showed that the iron-sucrose solution was the better. They have now given this solution to a large number of patients with iron-deficiency anæmia, and the fact that most were treated as outpatients is good evidence that reactions were few. The dose is gradually increased from 25 mg. of elemental iron on the first day to 50, 100, and 200 mg. on subsequent days. Beyond the 200 mg. level they found that reactions were disproportionately frequent (though NISSIM gave as much as 500 mg.). The solution was injected directly from a syringe into a vein and no following lavage was needed. A dose of 100 mg. of elemental iron should raise the hæmoglobin in the blood by 0·55 g. per 100 ml. (4% on the Haldane scale); and we know from animal experiment that intravenously injected iron is utilised quantitatively in the formation of hæmoglobin. But in the patient with a chronic iron-deficiency anæmia there is the added factor of depleted stores, and the extent of the depletion is unknown. SLACK and WILKINSON allow for this by adding 50% to the dose calculated from the hæmoglobin deficiency, giving 200 mg. daily until this total is reached. Further treatment is rarely required; but patients with chronic infections or chronic blood-loss—e.g., from ulcerative colitis—need still larger quantities. Using this scheme of dosage, they found that intravenous iron-sucrose fulfils all theoretical expectations: patients with iron-deficiency anæmia, even when completely refractory to iron by mouth, are rapidly and fully relieved; there is a striking reticulocyte response, and sore tongue, dyspnœa, and fatigue disappear with equal speed. The fact that iron-deficiency anæmia can be relieved so much more quickly by intravenous than by oral iron has also been used by Dr. GOVAN and Dr. SCOTT, who report this week their experience with intravenous iron-sucrose in the anæmia of pregnancy. They point out that the symptoms of anæmia often become serious only a week or two before term; and the practice has been to give these patients blood-transfusions, because iron by mouth, even if tolerated, will not raise the hæmoglobin enough in the short time available. They record that of 900 patients no less than 30% had gastro-intestinal disturbance that made oral iron treatment difficult, while 14·3% had iron-deficiency anæmia that did not respond satisfactorily to it. To patients in all these groups intravenous iron brought speedy relief.

Here then is a practical solution along lines that for some time have been obvious enough in theory. We can now treat successfully those refractory iron-deficiency anæmias that have previously defied us. It is unfortuuate that of the parenteral routes the intravenous has to be used; it is not too simple, particularly since the iron solution has almost the same depth of colour as venous blood, and we doubt whether under present conditions many general practitioners will undertake such treatment. This means that patients must go to hospital, though most can be treated as outpatients. An intramuscular technique is the obvious way out, but the difficulties of preparing iron salts for administration by this route are exceptionally great. Meanwhile the present iron-sucrose solution is not the last word, and improved, and perhaps more convenient, preparations are likely to come soon.

5. Cappell, D. F. *J. Path. Bact.* 1930, **33**, 175.

Circulation of Blood in Healthy Tissues

HISTORICALLY, the detailed study of the functioning cardiovascular system began with the heart and thereafter embraced in turn the arteries and arterioles, the small peripheral vessels, and the blood-depots and veins. The physiology of the small vessels first received major attention from EBBECKE,[1] in 1917, but owing to the war his work was largely overlooked in this country. For technical reasons he did not get down to precise observations on the capillaries; that was left for DALE and RICHARDS,[2] KROGH,[3] and others, whose statements excited great interest in the 1920's. KROGH ascribed the contraction of capillaries to the activity of supposedly muscular pericapillary cells, which he generously named after ROUGET, their first discoverer. However, HOOKER [4] had put forward an alternative suggestion—that the mechanism of capillary contractility was swelling of the endothelial cells themselves—and there was a gradual rise of opposition to KROGH's view. Many physiologists thought that ZWEIFACH's [5] micromanipulative studies of the minute vessels of the living frog clinched the argument against the Rouget-cell theory, and in 1940 the researches of SANDERS, EBERT, and FLOREY [6] on the new-formed vessels in the rabbit's ear chamber seemed to show that capillary occlusion was effected, spontaneously or under nervous stimulation, by swelling of endothelial cells, much as HOOKER had supposed. But the matter was not so simple as that. In the first place, as W. M. BAYLISS pointed out as early as 1923, it was difficult to define a "capillary" from either the anatomical or the physiological aspect. Secondly, physiologists as a whole were unaware of, or had forgotten, various observations, such as LEONARD HILL's,[7] which should have warned them that the capillary bed is composed of structurally and functionally very dissimilar vessels. Next, the peripheral vascular fields studied had usually been far too limited in extent, and complicating factors (trauma, cooling, drying, colloid variations) had not been adequately excluded. Lastly, many of the technical procedures employed had been too clumsy for the proper study of the circulation in very small blood-vessels.

The more recent researches which have gone far to remove these objections have almost all been by Americans; here we may perhaps concentrate on the findings of ROBERT CHAMBERS and B. W. ZWEIFACH because they have produced from them a schema which can be tested against both past and future observations. CHAMBERS, long known for his pioneer

1. Ebbecke, U. *Pflüg. Arch. ges. Physiol.* 1917, **169**, 1.
2. Dale, H. H., Richards, A. N. *J. Physiol.* 1918, **52**, 110.
3. Krogh, A. The Anatomy and Physiology of the Capillaries. New Haven, 1922.
4. Hooker, D. R. *Physiol. Rev.* 1921, **1**, 112.
5. Zweifach, B. W. *Anat. Rec.* 1934, **59**, 83.
6. Sanders, A. G., Ebert, R. H., Florey, H. W. *Quart. J. exp. Physiol.* 1940, **30**, 281.
7. Hill, L. *J. Physiol.* 1920, **54**, 93P.

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work with micromanipulative techniques, transmitted his skill to his pupil, ZWEIFACH, and during the last fifteen years the latter, partly in coöperation with CHAMBERS and others, has applied it to the study of the small vessels in situ.[8] The regions studied have been the skin, tongue, mesentery, and intestinal wall of the frog; the ear and mesentery of the mouse; the interdigital web, scrotum, and mesocæcum (meso-appendix) of the rat; the ear, corneoscleral junction, and mesentery of the rabbit; the mesentery and omentum of the cat and dog; and unspecified nictitating membranes. Limiting factors have been the needs for avoiding trauma (hence the regrettable exclusion of mammalian skeletal muscle) and for getting a sufficiently wide peripheral field. Of the regions listed, those most suitable for observation of the small vessels, with or without micromanipulative intervention, have been the mesocæcum of the rat and the omentum of the dog. Within the range which has been studied, there is a relative autonomy of the peripheral blood circulatory bed from metarteriole to collecting venule, both included. The metarteriole communicates with the venule through an ever-patent capillary vessel, and the whole of this direct arteriovenous conduit is styled the thoroughfare channel; its metarteriolar portion has smooth muscle in its wall. At intervals in its proximal part precapillary vessels are abruptly given off, and these have smooth muscle at their beginnings but not elsewhere; when this muscle contracts endothelial ridges partially occlude the openings from the thoroughfare channel into the precapillaries, so that blood corpuscles cannot pass. The precapillaries give rise to the true muscle-free capillaries, and from these the muscle-free postcapillaries pass, to enter at acute angles the muscle-free venular end of the thoroughfare channel. Independently of variations in calibre in the arterioles, the metarteriolar and precapillary musculature undergoes relatively slow contractions and relaxations—i.e., this part of the vascular bed exhibits what CHAMBERS and ZWEIFACH call "vasomotion." During the contractions blood passes through the thoroughfare channels alone, whereas during the relaxations it enters the precapillaries and true capillaries also. The musculature normally contracts in response to vasoconstrictor nerve impulses (there is at present no evidence for vasodilator ones) or to the local application of adrenaline, but the response is temporarily reduced, or even abolished, through the action of metabolites if the tissue is active; in this way the blood-supply is adjusted to the tissue needs. When the flow of blood into the capillary area is cut off, by contraction of the precapillary sphincters, the true capillaries do not empty but serve as conduits for the passage of fluid from the tissues to the venule; the relatively fast blood-stream in the thoroughfare channel is thought to aid such drainage from the postcapillaries because of their acute angles of entry into the venule.

We thus have a new concept of the peripheral circulation with the basic needs of the tissues served by thoroughfare channels which vary in their degree of patency, but are always in some measure patent. When the tissue needs rise above this basic level blood periodically passes via the precapillaries into the true capillaries, and this passage is increased in amount and in duration by the refractoriness induced by tissue metabolites in the smooth musculature of the metarterioles and of the precapillary sphincters. It has yet to be shown that the schema proposed by ZWEIFACH and CHAMBERS is of universal application; meanwhile, it is a major thought-stimulating contribution, derived from years of extremely careful work, to our ideas on the tissue blood-supply and its regulation.

8. Zweifach, B. W. *Amer. J. Anat.* 1937, **60**, 473; *Anat. Rec.* 1939, **73**, 475; *Cold Spring Harbor Symposia on Quantitative Biology*, 1940, **8**, 216. Zweifach, B. W., Kossmann, C. E. *Amer. J. Physiol.* 1937, **120**, 23. Chambers, R. *Nature, Lond.* 1948, **162**, 835. Chambers, R., Zweifach, B. W. *J. cell. comp. Physiol.* 1940, **15**, 255; *Amer. J. Anat.* 1944, **75**, 173; *Physiol. Rev.* 1947, **27**, 436.

Annotations

HIRSCHSPRUNG'S DISEASE

IN 1886 Hirschsprung, of Copenhagen, gave us the clinical picture of the disease that bears his name. The following sixty years saw many attempts to ascertain its pathogenesis and to devise satisfactory treatment, but only lately has progress become encouraging. Ehrenpreis[1] in 1946 produced evidence that the dilatation of the colon is not congenital but develops weeks or months after birth. He defined megacolon as a dysfunction of evacuation, of unknown origin. A disturbance of autonomic innervation of the colon seemed to him very probable but not proven, for neurohistological investigations since 1901 had given contradictory results. Last August the American pædiatric surgeons Swenson and Bill[2] reported that suitable methods of radiography reveal a "spastic" segment of colon distal to the dilated part, and they concluded, on clinical grounds, that this obstructive narrowing is responsible for the dilatation. The rational treatment, they believe, is to resect the distal spastic segment, and they therefore introduced rectosigmoidectomy for Hirschsprung's disease. The probable cause of the spasticity was indicated by Zuelzer and Wilson,[3] also in the United States, when they reported segmental aplasia of ganglion cells of the myenteric plexus in several infants with acute intestinal obstruction; but their findings in chronic megacolon were not uniform. Meanwhile a research team had formed at the Hospital for Sick Children, Great Ormond Street, and the evidence that Dr. Martin Bodian and his colleagues presented on Dec. 1 to the surgical section of the Royal Society of Medicine appears in full in the paper we publish this week. They attribute some of the discrepant findings of previous investigators to the assumption that all cases of idiopathic megacolon are cases of Hirschsprung's disease. They reserve the latter term for the condition in which a contracted segment of bowel can be demonstrated with X rays, and in all the 17 cases of this kind that Dr. Bodian has examined histologically he has found complete aplasia of parasympathetic ganglion cells in the autonomic plexuses of the distal segment. Applying Swenson and Bill's principle of treatment by rectosigmoidectomy, with a modified technique, Mr. Stephens has had gratifying early results. We understand that none of the cases reviewed at Great Ormond Street have shown the dilatation of ureter or bladder that has sometimes been reported in association with megacolon, and for this reason Dr. Bodian and his colleagues do not speculate as to how such a condition might be related to their findings in the gut.

Though the effect of treatment on a chronic disease has to be judged over a period of years, a useful advance will have been made by the present work even if it does no

1. Ehrenpreis, Th. *Acta chir. scand.* 1946, **94**, suppl. 112.
2. Swenson, O., Bill, A. H. jun. *Surgery*, 1948, **24**, 212.
3. Zuelzer, W. W., Wilson, J. L. *Amer. J. Dis. Child.* 1948, **75**, 40.

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more than differentiate Hirschsprung's disease from the residual group of idiopathic megacolon. The radiographic findings and clinical picture should serve to distinguish those cases that are likely to prove mild, and to respond to conservative treatment, from cases of classical Hirschsprung's disease in which treatment should aim at overcoming the obstruction caused by a narrow distal segment.

CHILDREN AND THE FAMILY

Dr. René A. Spitz has shown that when a young child is separated from its mother its development slackens and it may sink into apathy and despair[1]; and studies of delinquent older children often bring to light a history of separation from the mother in infancy or early childhood.[2] Some of these delinquents fall into the class of "affectionless thieves." Knowing this, it is perhaps surprising that we so often prescribe removal from the family as treatment for the delinquent child; for though the older child probably stands up to such separation better than the very young one, the experience can nevertheless be damaging. Dr. Melitta Schmideberg,[3] argues that the money we spend on maintaining a delinquent child in an approved school or borstal could often be laid out more wisely in helping his family to arrange their lives a little better. "It is a far happier solution to help the parents to be better parents than to take away their children." This is most often true, perhaps, in cases where the child is removed to a hostel or institution because he is "in need of care and protection"; for, with the child, affection counts more than the opportunity to be clean and well fed in unfamiliar and often affectionless surroundings; and a dirty careless neglectful mother is not necessarily unloving. Dr. Schmideberg's experience has been similar to that of the subcommittee of the Women's Group on Public Welfare, which lately reported on the child neglected in his own home.[4] They found that the parents, and especially the mother, were more usually poor, incompetent, ill, or fatigued, than deliberately neglectful or cruel.

Some children in need of care and protection are sent to approved schools; and Dr. Schmideberg regrets the support the Curtis Committee gave to this practice. However good the atmosphere of an approved school may be, it is still largely punitive; and the child will inevitably come into contact with those who have a criminal or psychopathic history. To place a young girl in the society of those who have been detained for promiscuity, and to confront her suddenly with such aberrant aspects of sex as homosexuality and venereal disease, cannot be called a good example of care and protection. Nor is Dr. Schmideberg easy in her mind about the way many approved schools and hostels for difficult children are run. Staff are few, and many of them, she thinks, are unsuitable; magistrates seldom know fully the conditions in homes and hostels to which they send children on probation, and in some of these the young people work very hard at commercial tasks—laundry, dress-making, farming—without remuneration, all proceeds going to the institution. Religious hostels sometimes impose an almost conventual life on the children; yet it is not possible to generalise, for she notes that there are some excellent religious institutions making use of modern psychological and social methods.

At present too many children are removed from home and then—after months or years—sent back to the unsatisfactory environment. Surely some attempt should first be made to treat the family as a unit, and the delinquency of one member as a symptom of sickness in the whole. To send the parents to prison and the child to an institution is like dismembering a patient to cure his rheumatic pains. If the child must be removed, he generally does better, Dr. Schmideberg finds, in a well-chosen foster-home than an institution. But if we are to have institutions she would like to see them planned to meet the needs of different types of children; and there is a special need for small hostels where children could be placed temporarily. Staff in institutions should be carefully selected, well trained and properly paid. Finally, more nursery schools, playgrounds, and holiday camps for children, more rest homes for mothers, better hostels for adolescents, and centres where children and parents could turn for advice, would all, she believes, reduce delinquency and make good citizens of the coming generations.

1. See *Lancet*, 1948, ii, 106.
2. *Ibid.* 1945, ii, 715.
3. Children in Need. Published for the Psychological and Social Series Ltd. London: Allen & Unwin. Pp. 196. 12*s.* 6*d.*
4. The Neglected Child and His Family. London, 1948. See also *Lancet*, 1948, ii, 63.

THE AXILLARY INLET SYNDROME

SYMPTOMS commonly arise in the arm from compression of the subclavian vessels and of the roots and trunks of the brachial plexus as they pass from the neck to the axilla. In such cases there may be no radiological evidence of a cervical rib or of gross abnormality of the first rib; and the compression has been attributed to a number of factors. Considerable importance has been attached, particularly in the U.S.A., to spasm of scalenus anticus[1] as one cause of compression; while another is compression between the clavicle and the first rib in the so-called costoclavicular syndrome.[2] Kirgis and Reed,[3] who have made detailed dissections of the neck in 56 cadavers, suggest that too much weight has been given to the rôle of scalenus anticus, the ordinary fibres of which are not in a position to compress the subclavian vessels and nerve-roots. If spasm of this muscle plays any part in producing symptoms it is by elevating the first rib and thus compressing the lower trunk of the plexus and possibly the subclavian artery. In a number of bodies scalenus anticus was found to have aberrant fibres, arising from the inferior margin of the grooves of the transverse processes in which the issuing nerve-roots lay, and passing anteriorly to join the main body of the muscle. Contraction of these fibres might pinch the nerve-root immediately beneath them. Scalenus medius seemed to these workers important as a possible cause of symptoms; in almost all the dissections the lower trunk of the plexus rested on the inferior part of the anterior surface of this muscle, and they thought that when the muscle contracted the sharp anterolateral border might compress the lower trunk. Scalenus minimus was demonstrated in 55% of the dissections; it arose from the transverse process of the 7th cervical vertebra and was inserted into the first rib posterior and somewhat lateral to the attachment of scalenus anticus, passing behind the subclavian artery and in front of the lower roots of the plexus. If this muscle is abnormally large it may act as one jaw of a vice, the lower trunk of the plexus being compressed between it and scalenus medius.

These observations, though made on unselected cadavers, indicate that several mechanisms may help to initiate symptoms. Certainly when symptoms are severe enough to justify operation, the subclavian vessels and the lower roots and lower trunk of the brachial plexus should be thoroughly explored to discover where exactly compression is taking place. Division of scalenus anticus cannot be considered a satisfactory procedure

1. Ochsner, A., Gage, M., DeBakey, M. *Amer. J. Surg.* 1935, **28**, 669. Swank, R. L., Simeone, F. A. *Arch. Neurol. Psychiat.* 1944, **51**, 432.
2. Falconer, M. A., Weddell, G. *Lancet*, 1943, ii, 539. Walshe, F. M. R., Jackson, H., Wyburn-Mason, R. *Brain*, 1944, **67**, 141.
3. Kirgis, H. D., Reed, A. F. *Ann. Surg.* 1948, **127**, 1182.

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for all cases: it may relieve symptoms (probably by allowing some depression of the first rib), but it may also aggravate them.[4] The term "scalenus anticus syndrome," with its narrow connotation, should be discarded. "Thoracic-outlet syndrome" is a possible alternative; but the structures involved are really above the thoracic outlet and run either towards or, in the case of the subclavian vein, from the axilla. "Axillary inlet syndrome" seems to be a better name for the group of cases with compression of the neurovascular bundle by structures other than a bony cervical rib.

WEATHER AND ILLNESS

COMPARED with our ancestors we pay remarkably little attention to the effect of weather changes on body and mind: the subject is out of fashion. The climatic factors associated with respiratory catarrh have been enumerated [5]; the correlation of climate with the mortality of certain diseases in the U.S.A. has been rather inconclusively worked out [6]; and Corkill [7] has related the onset of cerebrospinal fever in the Sudan to lack of humidity, illustrating his thesis with graphs showing number of cases, daily temperatures, humidity, and rainfall. But in these and similar inquiries the difficulty remains that these meteorological factors are comprehensive phenomena of not very definite onset and location in time and space and probably contain a multiplicity of more definite factors which need sorting out. At the International Congress of Rheumatism and Hydrology in London before the war [8] Edstrom, of Lund, suggested that the most significant feature of a climate might be its abundance of cyclones and anticyclones, and de Rudder, of Frankfort-on-Main, drew attention to the importance of the alternation of cyclones and anticyclones and their lines of aerosol interface.

The weather of the western seaboard of Europe consists chiefly of a succession of pressure systems advancing from the Atlantic. As each system moves eastward its winds blow round it, those of cyclones or depressions (associated with bad weather) blowing in an anticyclonic or anticlockwise direction, and those of anticyclones (associated with good weather) blowing in a cyclonic or clockwise direction. The oxymoron perpetrated by this nomenclature is due to the fact that these pressure systems were first named in the southern hemisphere, where their winds blow in the opposite directions. Each system can be regarded not as an upright wheel running along a road but as a sort of catherine wheel laid flat and sent spinning across a sheet of glass; but perhaps its nearest analogy is a whirlpool which is formed immediately downstream from the pillar of a bridge and passes gradually down the river. For purposes of medical meteorology the drawback is that a cyclone is too dispersed, and its limits too indefinite, for us to pin it down as a responsible factor in causing disease. Luckily, however, cyclones form mainly along fronts—e.g., the polar front—where a mass of cooler air meets a mass of warmer air. Therefore, as it spins round, a cyclone carries a mass of warmer air to meet a mass of cooler air, thus forming a front of its own stretching from the centre of the depression to the periphery, like a spoke of a wheel. Simultaneously a mass of cooler air from the more northerly sector of the disturbance is dragged into the system and forms another "spoke"—a cold front which follows the warm front and may in turn be followed by still colder fronts. Each front is usually accompanied by rainfall. Thus, normally, a widespread fall of rain associated with a warm front is soon followed by other widespread falls of rain associated with the following cold fronts. Often, however, the first cold front catches up with the warm front (as if a spoke of a revolving wheel were to catch up and fuse with another), and there is but one rainfall for these two fronts. This is known as an occlusion.

It is to these meteorological minutiæ that Mouriquand and Charpentier [9] have turned in an attempt to elucidate the connexion, if any, between weather and illness. They noted that five out of six children, aged 6–14 years, with tuberculous meningitis, who had been treated with streptomycin for several weeks or months and had considerably improved, suddenly, on the night of Sept. 20–21, 1947, became restless and had violent headaches and vomited, one of them even becoming delirious. The one child who did not show any such disturbance had already so far recovered that no sign of meningism remained. Mouriquand and Charpentier were acquainted with Sommer's [10] observation that the babies in a clinic at Lyons had been restless for several hours during the passage of an occlusion. So they consulted the meteorological charts for the district and found that a succession of four cold fronts had passed through on the night of Sept. 21–22. They also inquired how the babies in the clinic had fared, and were told that, for a few days before and a few days after the upset of the children with meningitis, the babies had likewise been restless, the time of maximal restlessness coinciding with that of the children with meningitis. The official meteorologist for the area gave the following information: no front in the district on Sept. 14 and 15; a cold front on the night of Sept. 16–17 (when babies in the clinic were restless); no front on Sept. 18; fronts on Sept. 19 (the sister in the babies' clinic had noted: "As on the day before yesterday, the babies are crying. Sleeping lightly, they are difficult to look after"). Next followed the disturbance already described. Order was restored in the babies' clinic and among the children with meningitis on Sept. 26, and the latter children continued to improve as before. On Sept. 26, 27, and 28 the meteorological charts showed an absence of fronts in the area. Surely such fronts had passed before; so why had the children with meningitis not been upset previously? A search of the meteorological records showed that, as regards change in temperature, the successive fronts of Sept. 21–22 had been unusually severe.

BIOPSY OF THE GASTRIC MUCOSA

THE invention of the flexible gastroscope was naturally followed by attempts to devise additions for the purpose of biopsy. One such attempt was made in 1946 by Kenamore, Scheff, and Womack, who designed a biopsy forceps for use in conjunction with the Schlindler gastroscope. The method has not found much favour in this country, because in the diagnosis of localised lesions of the stomach biopsy may be actually misleading. The principal diagnostic difficulty confronting the gastroenterologist is in distinguishing between peptic ulcer and early ulcer-carcinoma. This difficulty is not solved even by exploration, for the surgeon is commonly in doubt whether to perform a subtotal gastrectomy for the cure of ulcer, or a radical type of operation for the extirpation of cancer. To depend upon biopsy—even if a selected area of the ulcer could be obtained—would be to court disaster. In doubtful cases, where all accepted diagnostic tests fail, the truth is revealed only after operative removal, by histological examination of the whole ulcer area.

In the field of research, however, and especially in the study of diffuse lesions of the gastric mucosa associated with abnormalities of the blood, biopsy makes some appeal. On another page Dr. Wood and his colleagues describe a flexible biopsy tube which, though used

4. LeVay, A. D. *Lancet*, 1945, ii, 164.
5. Copeland, A. J. *Lancet*, 1941, i, 742.
6. Herrington, L. P., Moriyama, I. M. *Amer. J. Hyg.* 1938, **28**, 396; *Ibid*, **29**, 111.
7. Corkill, N. L. *Lancet*, 1939, i, 1203.
8. See *Lancet*, 1938, i, 801.
9. Mouriquand, G., Charpentier, R. *Pr. méd.* 1948, **56**, 767.
10. Sommer, M. Lyon thesis, 1937, cited by Mouriquand and Charpentier.

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blindly, has enabled them to obtain sufficient gastric mucosa for detailed histological study in 55 out of 83 attempts; though somewhat inconvenienced, the patients were apparently unharmed. In one of the cases described gastric biopsy showed hæmosiderin in the parietal and chief cells of the stomach; liver biopsy showed changes typical of hæmochromatosis; and skin biopsy a little hæmosiderin in the sweat glands. In another case biopsy revealed atrophic gastritis associated with pernicious anæmia; and of two further cases one was found to have chronic atrophic gastritis with a normal blood picture, and the other chronic gastritis whose nature is unspecified.

On whether findings of this order justify the means of obtaining them, opinion will differ; but most would agree that the procedure should be confined to centres carrying out organised research into changes in the gastric mucosa.

HEATING OF HOUSES

THE problems of housing have held the imagination of our people for nearly a generation. At the end of the first world war the shortage of houses became acute, and one Administration after another made its contribution to the building programme. From 1930 onwards the attention of the Government was directed in turn to slum clearance and to the relief of overcrowding; and considerable progress was made before the return of war cut short this great social effort.

During the whole of the inter-war period earnest attempts were made to meet the demand for houses of low cost, but relatively little thought was given to the kind of home that ought to be provided. Comfort and amenity took a subordinate place in planning, with the result that traditional designs, offering open hearths as the sole means of space heating, were almost universal. Few attempts were made to apply scientific methods in assessing the efficiency, or in calculating the relative costs, of different types and combinations of heating appliances. Recently the Building Research Station, working under the general direction of the Department of Scientific and Industrial Research, has succeeded in supplying authoritative data on which estimates of efficiency and economy in warming small homes can be based. A team of workers led by Mr. Richard Eve has now begun to publish [1] the results of a thorough investigation carried out in a group of trial houses at Abbots Langley. The houses were unoccupied at the time of the preliminary study, but the staff used the various appliances in such a way as to reproduce the ordinary conditions of life for a family of father, mother, and two children. They examined three main types of space heating: the "partial," with a fire in the living-room and no heating arrangements in the bedrooms; the "two-stage," with limited background heating in two or more bedrooms, and provision for "topping-up" with gas or electric fires as required; and the full central heating up to 65°F in every room. Under the experimental conditions each house was expected to provide for 250 gallons of water at 140°F per week; with warmth at 65° in the living-room for eight hours a day, and 60° in the kitchen. The bedrooms were warmed to the same extent, so far as the heating appliances allowed.

In carefully controlled observations it was found that the space heating actually obtained improved from the partial to the whole house heating; and that there was no great difference between the two-stage and central heating in efficiency, except that the latter maintained better levels in really cold weather. The main point, however, was that full central heating was substantially cheaper in maintenance than the other types, while giving at the same time much greater uniformity in space warming. In capital costs full central heating was more expensive to install, but owing to its efficient and economical use of fuel the extra initial expense would be balanced in about twenty years.

These elaborate studies have at last brought the problems of space heating under scientific measurement, and the results of continued research will be watched with interest, because hitherto we have had to content ourselves with opinion based on guesswork.

1. *J. R. Inst. Brit. Arch.* November, 1948.

POTENTIATION OF STREPTOMYCIN

IODIDES have long been known to cause tubercle bacilli, previously absent, to appear in the sputum of patients with pulmonary tuberculosis; and for many years they have also been used to promote the solution and absorption of fibrocaseous lesions in the lungs of the tuberculous. These facts have led Woody and Avery [1] to test the combined action of potassium iodide and streptomycin against established tuberculosis in guineapigs. After excluding any possible effect of potassium iodide on the antibiotic action of streptomycin, they injected the two drugs into guineapigs inoculated with a suspension of tubercle bacilli (H37RV). The controls were inoculated guineapigs receiving either no treatment at all, or potassium iodide alone, or streptomycin alone. All the animals were killed at the end of four weeks. On gross examination the untreated guineapigs and those treated with potassium iodide showed heavy tuberculous infection of all viscera, and the streptomycin guineapigs showed some spread to the organs; but in those treated with potassium iodide as well as streptomycin the organs were entirely free from infection. A survival experiment gave comparable findings, the mortality-rate after fifteen weeks being lowest in the animals that had both streptomycin and potassium iodide.

This observation is of considerable interest. If it could be shown clinically that the two drugs, when given together, are more effective than streptomycin alone it should be possible to reduce the dose of streptomycin for the treatment of tuberculosis, and so diminish the undesirable side-effects. At present the daily effective dose of streptomycin is supposed to be 2 g.; but evidence is already accumulating that it may be as small as 1 g. If the dose could be cut still further the side-effects might be negligible; and in countries, such as Britain, where streptomycin is scarce more patients could have the benefit of it.

1. Woody, E., Avery, R. C. *Science*, 1948, **108**, 501.

SPECIALISTS AWARDS COMMITTEE

THE Minister of Health and the Secretary of State for Scotland, acting on the recommendations of the Spens Committee, have appointed a committee of 14 members to advise "which specialists engaged in the National Health Service should receive awards for professional distinction, having regard to the desirability that 4% of the number eligible should receive the highest award, 10% the second award, and 20% the third award." The members are:

Lord Moran, P.R.C.P. (chairman), Sir Horace Hamilton (vice-chairman), Mr. V. Zachary Cope, F.R.C.S., Prof. G. B. Fleming, F.R.C.P., Sir Gordon Gordon-Taylor, F.R.C.S., Mr. J. M. Graham, F.R.C.S.E., Sir David Henderson, F.R.C.P., Sir Edward Mellanby, F.R.C.P., F.R.S., Mr. J. F. Mountford, Sir Harry Platt, F.R.C.S., Prof. A. L. Robinson, F.R.C.O.G., Dr. J. H. Sheldon, Sir Lionel Whitby, F.R.C.P., Mr. J. M. Wyatt, F.R.C.O.G., Mr. T. B. Williamson, of the Ministry of Health, is secretary. Eleven members of the committee have been nominated by the Royal Colleges and the Scottish Royal Corporations, one by the Medical Research Council, and one by the universities' committee of vice-chancellors and principals.

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Special Articles

THE PSYCHOPATH IN OUR MIDST

A Danish Solution

STEPHEN TAYLOR
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IF one could assess the human misery produced, it might well be found that the psychopath has a blacker record than either the neurotic or the psychotic. The neurotic knows he is ill, is only too willing to seek medical aid, and is usually prepared to coöperate; the psychotic's illness is patent to his friends, they can persuade or compel him to receive treatment, and his detention can continue until he is well; with the psychopath, however, it is always the rest of the regiment who are out of step. He has been let down or unfairly treated; it is not he but society which must put itself right; as for seeing or coöperating with the doctor, it is an insult. So the psychopaths in our midst go through life creating trouble. In the factory or office, in the club or society, in the hospital or nurses' home, they build up around themselves a circle of discontent, not the divine discontent of the rebel or reformer, but the narking, carping, querulous complaining of men and women with a grievance against society.

I must confess to a fascination in the psychopath, ever since I realised that Hitler and his gang were psychopathic criminals carried to the top on a wave of uncured unemployment. They had all the superficial attraction which makes the psychopath the ideal "con" man. And in Trevor-Roper's book, *The Last Days of Hitler*, one can study the miserable spectacle of the psychopath in defeat. One of the problems of politics is to keep psychopaths away from the top; and in Britain we have solved it by making the top comparatively unattractive. No Prime Minister in our history has been unreservedly popular. His powers are circumscribed by law and tradition, and his every action can be called in question by the Parliamentary Opposition. His house and his income are comparatively small, his work arduous, his leisure disturbed, and his tenure of office always dubious. Added to this, the road he must tread to reach his position is one of endless patience, appalling hours, and never-ending fraternity with his fellows. Had Hitler secured election to the House of Commons, he would soon have found himself on the bench below the gangway reserved de facto for independents, where infrequency of attendance is subject to no party discipline, and where shelving of personal prejudice for the common good is never necessary.

But this is no solution to the problem of the psychopath in everyday life. Psychopathy is the hardest diagnosis to pin-point. Its dividing line from genius is never easy to discern. Carlisle in the home was a psychopath; but given pen and paper he was capable of vast enrichment of human thought. Had psychopathy been a certifiable complaint, Nelson might have languished in some Georgian Bedlam, and Bunyan never been allowed the means of producing *The Pilgrim's Progress*. Perhaps genius and psychopathy are differentiated by the capacity of the genius to stick to things, to persevere, and to succeed in getting part, if not all, the regiment to accept his rhythm of marching as correct.

Because of difficulty of diagnosis, because genius must at all costs be preserved, any widespread medical or psychiatric treatment of psychopathy is out of the question. For the most part, we must grin and bear our psychopaths, working out for ourselves the best method of coping. Often neglect is the best remedy, and only rarely is something more violent effective. Psychopathy flourishes on rows, and many a psychopath has built up a position simply on the reputation for an ungovernable temper. But this is rough pragmatic treatment only, the best we can manage in the present state of knowledge. I had almost given up hope of getting further with the matter until a few weeks ago when I heard behind me the slam of the doors of the Psychopathic Prison at Herstedvester, some fifteen miles out of Copenhagen.

THE DANISH LAWS

The Danes are a rational people; they have even managed not to reason away their sense of humour. In 1881 they gave up capital punishment, though they did not repeal the law till 1933. Yet they have reintroduced execution for their traitors; 15 have already been dealt with thus, and another 15 or so are awaiting the investigation of their appeals. No nation is socially perfect, and certain further Danish weaknesses will become apparent inside the Psychopathic Prison. But they have come further along the road to the good life than most of us. And in this prison we may catch a glimpse of the future. In this prison the Danes have recognised that "hypocritical matrimonial defrauders, brutal child violators, and dangerous incendiaries" are fit subjects not for punishment but for treatment; though treatment, to be effective, must be a stern discipline.

The Danish criminal law of 1930 contains no McNaghten Rules. But two sections of it deal with mental upset and crime. Section 16 says no person who has committed a crime shall be subject to any punishment if, at the time of the deed, he was irresponsible on account of insanity, or a similar condition of mind, or a high degree of mental deficiency. Such cases go to the ordinary mental hospitals, and Denmark has no equivalent of Broadmoor. Under section 16, some 25 patients a year are sent to mental hospitals by the courts. Some are true psychotics, perfectly suitable for mental hospital treatment; but others are psychopaths with psychotic episodes, disturbers of other mental patients, whose proper home is the psychopathic prison.

Section 17 of the Criminal Law deals with mentally abnormal criminals not covered by section 16. It covers those who, at the time of the deed, were suffering from some more permanent upset yet who could not be said to be irresponsible. Mental conditions covered include mental underdevelopment, mental weakness, or derangement of mind including sexual abnormality. Having decided, with the aid of a medical certificate, that a person falls under section 17, the court then has several alternatives open to it. If it decides the individual will benefit from punishment, he or she can be sent to an ordinary prison. Alternatively they may be sent to a mental hospital, a home for inebriates, or to the psychopathic prison.

Sentence to the psychopathic prison is indeterminate, a point of great importance. Release can only be sanctioned by the same court which convicted the prisoner. This is almost always done on the recommendation of the medical superintendent, though the prisoner has a trustee outside who may also petition for his release. Release is always subject to parole and the length of parole is not defined. Final release from parole is again on the order of the original court.

Thus at Herstedvester are collected what the lay person might justly describe as a sample of the wickedest people in Denmark. They are confined there for the benefit of society, until such time as the medical superintendent judges they can safely be released. The miracle of Herstedvester is that they can claim a 50 per cent cure-rate.

Before examining how this miracle is achieved, the defects of the arrangement may be noted. Some psycho-

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paths get into ordinary prisons without being diagnosed; others get there because the courts decide they will benefit from ordinary punishment; others, as already mentioned, get put into mental hospitals. These psychopathic inmates of the mental hospital and the ordinary prison differ in no way psychiatrically from the patients in the psychopathic prison. There appears, therefore, to be a need for some machinery whereby a criminal, who is found in prison or in mental hospital to be a psychopath, may be transferred to the psychopathic prison.

It has often been suggested that the only way to deal with psychopaths is by dilution, that each social group must carry its quota as best it can, and that concentration in one place would result simply in chaos. Such a policy is a doctrine of defeat. The diluted psychopath inevitably becomes a focus of misery and discontent. Decent folk are thrown out of gear, and much time is wasted coping with the artificial emotional problems which the psychopath glories in creating. Dr. G. K. Stürup, the superintendent of the Psychopathic Prison, says: "At Herstedvester, for a number of years, we have had from 120 to 150 psychopathic detainees and prisoners, and they have caused considerably less trouble than when they were scattered over various hospital wards and prison wings, among more ordinary prisoners. Here the widely divergent personality types hold each other in check, the staff gradually get sufficient training and experience, and modes of treatment can be laid down giving comparatively fixed limits to the individual displays that may occur. He that does not work will not earn money and so must go without tobacco, newspapers, and cakes on Sundays, just as in ordinary life. These are small things, but it is quite unpleasant to watch one's more industrious fellows reaping the benefits of their diligence" (Stürup et al. 1948).

A PRISON FOR PSYCHOPATHS

The Psychopathic Prison stands behind a high plaster-covered white-painted wall. But once inside the wall, it is more reminiscent of a modern mental hospital than a prison. The gardens are beautifully laid out and rich in flowers. There are no exercise yards. No block is more than two stories high, and all windows are full-sized. Over the administrative offices are the rooms for the most violent patients. As is general in Denmark, there are no padded rooms and no rooms without beds. For the most violent patients, the beds are fixed to the floor in the middle of the room, canvas straps round the stomach anchor the patient to the bed, and massive leather gloves, without fingers, firmly attached round the wrists, prevent self-injury and the destruction of clothes and bedclothes. One prisoner receiving such treatment was a gross schizophrenic, a leading Danish traitor. There were also two noisy manics differing in no way from their mental-hospital counterparts. These patients are either misdiagnoses by the courts, or psychopaths with psychotic episodes.

The non-violent patients live in villas, usually in single rooms but sometimes in rooms for three or four. The day rooms are pleasant and in each villa there is a large carpentry room, in which patients can make additions to their own furniture in their free time; much of this furniture is of the highest quality. Radio sets, carpets, and pictures are permitted, and those who care to decorate their rooms with pin-up girls and nudes may do so. Dr. Stürup wisely says that this is better than having them on the backs of the pictures; besides, public display encourages improvement in taste, even in this direction.

All patients who are able to do so work an 8-hour day, at gardening, printing, bookbinding, carpentry, toy-making, tailoring, or building repairs. Wherever possible there is piece-work, and average earnings are 10*s*. a week. Half of this may be spent, the other half being saved until release. As the capacity to hold down a job in the outside world is one of the criteria of cure, patients have this extra incentive to make a success of the jobs they tackle.

There is a lively club life—including sports, bridge, chess, stamp-collecting, a marionette theatre, and amateur theatricals. There are also study circles and correspondence courses available. Again, successful use of leisure is another criterion of cure.

On admission, every patient is subjected to a full physical and psychiatric examination. His statements are checked against his police record, and he is politely but firmly corrected every time he is found to be lying. He has to be given the feeling he is responsible for his own future, and that, though the doctor will help him to bear his burdens, he alone can deliver himself from Herstedvester by his own efforts.

At first, most patients, accustomed as they are to ordinary prisons, are delighted with life at Herstedvester. This they feel is too good to be true. But after two or three months they suddenly realise that they have no idea when they are going to get out. As a result a violent or sullen reaction begins. Dr. Stürup is convinced his only chance of getting under the skin of these people is to strike when they are in a state of emotional tension. All his staff are trained to spot these moments of strain, and to send for him at once. He then applies common-sense psychotherapy, explaining to the patient why he is feeling and behaving as he is. And slowly, the patients come to accept the possibility of a non-egocentric universe. No deep psychotherapy is attempted. In cases where it is needed—for example, exhibitionism—it is much better undertaken on an outpatient basis.

Almost all patients are recidivists, with serious crime records. The main crimes of the first 300 admissions were: theft 94, sexual crimes against children 88, confidence tricks 31, fraud 22, arson 16, exhibitionism 15, violence including homicide 13, "polycriminality" 11, and rape 10. There is little correlation between type of crime and psychiatric state: nearly 80% are true psychopaths, with or without added psychotic or neurotic episodes, or some degree of mental defect; 5% have organic disease of the nervous sytem, 8% are epileptics, and 12% are alcoholics.

The staff of Herstedvester consists of 4 psychiatrists (2 more are urgently needed), 2 nurses, 1 school-teacher, and 1 sociologist for welfare work with 3 assistants drawn from the ranks of the warders. The warders have had mental-hospital training, and the staff-patient ratio is 1 to 2. The welfare workers are of special importance, since they not only know the patients in prison but are responsible for all outside follow-up work while the patients are on parole. They have to travel all over Denmark, and their value to the patients is greatly increased by the fact that they themselves, like the great majority of patients, are drawn from the so-called working classes.

That, in brief, is the story of Herstedvester. The prison has also a small female wing and two outstations, one being run on minimum security lines. Yet most observers see the story quite distorted by one incidental feature. Each year a certain number of persistent sexual offenders at Herstedvester are castrated, and supplied with glass testicles (Wulff and Sand 1945). This process is nominally voluntary, but since it is often the only way to release, refusals are comparatively rare. Its results are claimed to be good, but much impartial psychiatric study is needed before it could be recommended. In the last twenty years, some 300 people in Denmark have been castrated. In the same period,

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some 2000 in mental-deficiency institutions have been sterilised; this is not done for eugenic reasons, but simply to make it possible for them to live in society without being a burden to themselves or others. Both these processes have logical justification. Whether they are morally or socially justifiable is another matter, on which I do not feel competent to pronounce.

CONCLUSIONS

Putting aside the questions of sterilisation and castration, I feel that Herstedvester is the most brilliant answer to the problem of human wickedness which has yet been devised. To take the scum of the prison population and to cure half of them is something I had regarded as impossible. As Dr. Stürup says, it is not a matter of making criminal psychopaths into normal people, but of making them into nice psychopaths who are capable of adapting themselves to ordinary life.

Herstedvester is something I believe we should copy. But it is wrong to expect the courts to diagnose psychopathy. The proper place for diagnosis is in the prison psychiatric clinic. But once transfer to the psychopathic prison takes place, the sentence should become indeterminate, for the possibilites of cure are entirely dependent on the prisoner having to work his passage. The conversion of an absolute to an indeterminate sentence is a serious matter, and it must be remembered it is as much for the good of society as for the prisoner; certification should perhaps therefore be done by a High Court judge, with the full criminal and medical evidence before him.

The old conception of the criminal lunatic is one we ought to get rid of at the earliest possible moment. Anyone charged with a crime who is in fact suffering from a psychosis should not be sentenced but certified and treated in an ordinary mental hospital. Criminal psychopaths should be sentenced in the ordinary way, diagnosed in prison, after careful and if necessary prolonged observation, and then transferred to a psychopathic prison on an indeterminate sentence, there to remain until (if ever) they are fit to return to society. We must face the fact that, with our present knowledge, a certain proportion of criminal psychopaths are completely incurable; for the benefit of society, they must be segregated indefinitely. But if it is possible to reclaim and convert into useful citizens something like half of the worst recidivists—and Herstedvester shows that it is—then it is our plain duty to get on with the job as quickly as possible.

Valuable though the work of criminal reclaiming is, the social significance of Herstedvester is much more profound. For here we have the first successful attempt at the scientific treatment of human wickedness. Outpatient psychiatric treatment of the really vicious criminal is almost always a failure, since the will to reform is as a rule completely absent. In Herstedvester, it is possible to develop the will to reform, since it is the only route of return to the outside world. Above all, in such a place, the codification of scientific knowledge about psychopathy can begin. Acquaintance between the psychopath and the psychiatrist has in the past often been nodding only. For the psychopath spurns the doctor, and seldom gets into the mental hospital. In those psychopaths whom society has decided must be withdrawn from circulation, we have a clinical pool in which we shall certainly catch fish with jewels in their mouths.

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HOW TO APPLY FOR MEDICAL POSTS

No amount of good advice can increase the number of successful candidates for medical posts, because there is only a limited number of jobs. Nevertheless, there are many unsuccessful applicants who feel frustrated because they do not feel they have made the best of their attempts, and those starting to apply for jobs are often uncertain of the best way of making their applications or conducting their interview. It is to these people that this article is addressed. The greater the efficiency of applications and interviews the more likely is it that the most suitable candidate will be elected. The advice given here applies in the main to posts at outside hospitals, for the junior appointments at teaching hospitals are made by staff who know the candidate already.

The three stages in obtaining an appointment are: (1) choosing a likely post, (2) composing a suitable application, and (3) interviewing the appointments committee.

THE CHOICE

The candidate is wise to ponder carefully over the advertisements in the medical press and restrict his choice to a few carefully selected posts. Do not apply for jobs you don't want, because candidates who turn up for interview and then decide they do not want the post are causing unnecessary work for appointments committees. Do not apply for a post "just to have a crack at it" when you have hardly any chance of success—it has a demoralising effect on a candidate to be turned down frequently. Choose a job that you really want and that you feel adequately equipped to perform.

It is a good idea to try and find out a little more about a post before you apply. You may have friends who have worked at the hospital concerned or known the chief with whom you will work; from them you may get helpful inside information. With a senior post it is quite justifiable to try and arrange a visit to the hospital and so meet the people you would work with and see the conditions and equipment of the department. Because of the "no canvassing" clause in advertisements many people are afraid to go near the hospital before the interview, though it is a perfectly reasonable thing to do.

THE APPLICATION

It is worth taking a lot of trouble to set out the application systematically, and to have it neatly typed and attractively presented. Remember that short lists are made from a large number of applications, and if good points are poorly presented they may easily be overlooked. Further, a slovenly application may give an impression of a slovenly applicant. Therefore the small expense of good paper and professional typing is worth while. Fresh typing looks much better than carbon copies or cyclostyled printing, and avoids giving the impression that the candidate is always applying for jobs. Here is an example of a systematic arrangement of a candidate's particulars.

The first page thus:

To the Secretary,
Central Regional Board,
Bevan Buildings,
W.1.

The Application of John Smith, M.D.,
for the Post of Medical Registrar
to the Cardiological Department,
St. Job's Hospital.

1, Leech Court,
Jan. 1, 1949. Systole Street, W.1.

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The second page thus:

Sir,

I have the honour to apply for the post of registrar to the cardiological department at St. Job's. My particulars are as follows:

Name: John Edward Smith.
Age: 30.
Nationality: English.
Place and Date of Birth: London. June 1, 1918.
Early Education:
St. Quinidine's School and Galen's College, Oxbridge.
Medical School:
St. Richard's Hospital.
State:
Married, with one child.
Academic Qualifications:

B.Sc. 1st class honours	1941
M.A., Oxbridge	1941
L.R.C.P., M.R.C.S., England	1942
M.R.C.P., England	1945
M.D., Oxbridge	1946

Academic Distinctions:

The Darwin Biology Prize (St. Quinidine's)	1936
Entrance Scholarship, Galen's College, Oxbridge	1937
The Osler Medal for Clinical Medicine	1940

Appointments at St. Richard's Hospital:

Clinical assistant to surgical outpatients	1942
Demonstrator, pathological department	1942
House-physician to Sir Bernard Bronchus	1943
Junior registrar to cardiological department	1944

Military Service:
1945–46 R.M.O. to The Marylebone Highlanders.
1946–48 Graded specialist attached to 693 General Hospital.
Demobilised 1948 with rank of major.
Other Experience:
Teaching.—I was demonstrator in anatomy for six months, Oxbridge, 1941. I have two years' experience of teaching and lecturing in elementary cardiology, 1944 and 1945.
Tropical Diseases.—I had considerable experience of tropical diseases in Burma and North Africa during my army service.
Languages.—I speak fluent Spanish and have a working knowledge of French.
Learned Societies:

Fellow of the Royal Society of Medicine (member of the cardiological section)	1945
Member of the British Medical Association	1942
Secretary to St. Richard's Medical Society	1943–44

Publications:
A Case of Struve's Disease. *St. Richard's Hospital Journal*, 1943.
Genetic Studies in Heart Diseases. *Journal of Cardiac Genetics*, 1947.
Prolonged Circulation Time in Albinos. *Proceedings of the Mackenzie Society*, 1948.
Referees:
Sir Bernard Bronchus, O.B.E., F.R.C.P., senior physician, St. Richard's Hospital.
Victor Valve, Esq., M.D., The Coronary Club, Heart Street, W.1.

With more senior posts a covering letter is often written, or the introduction on the second page is expanded to describe any reasons why the applicant feels he is specially suitable for the post. Many foreign doctors enclose with their application a long, boring, and irrelevant life-story including all their hardships and injustices. This cuts no ice.

Testimonials

In this example referees have been given, and therefore no testimonials are enclosed with the application. This practice is increasing steadily, and there is no doubt it is much more satisfactory than the old testimonial system.

The orthodox testimonial with its standardised phrases about "loyal and agreeable colleague" and "conscientiously recommend him for any post" usually carries little weight even if signed by a well-known name. The reason is that when a junior doctor asks his chief for a testimonial he expects as a natural right a glut of superlatives, and nearly always he gets it. A few men try to write honest testimonials, but it is very hard to write a just and true opinion of a doctor if that opinion is to be handed to the subject himself. Consequently, a convention has developed that every testimonial must be loaded with praise whatever the merits of its owner. Testimonials for that reason have become increasingly insincere and stereotyped and are treated with increasing disregard. Referees, on the other hand, can be written to and asked for a confidential report on a man, and their statements are much more revealing. If the advertisement for a post requires testimonials and/or referees, the candidate is wise to choose referees whether or not he sends testimonials as well. Before a candidate chooses a person as a referee he should obtain his permission to use his name for that purpose.

THE INTERVIEW

First, clothes. No committee consciously takes much notice of clothes, but it is advisable to look reasonably neat and clean and not to convey an impression of casualness—it cannot do harm to take a little trouble, and it may do good. Nevertheless don't "dress up," putting on clothes you never wear normally—a man who only wears a hard collar for interviews looks stiff and starched, and ill at ease, like a confirmation candidate or a choirboy.

Secondly, be natural. A candidate who tries to "put over" a planned impression reeks of insincerity. Do not try to think during each answer exactly what impression it will make. If somebody is obviously trying to be charming or to be confident, it is astonishing how unattractive he is. Your own natural self is almost always more attractive than the self you think the committee want you to be.

Don't be on your guard. Those interviewing you want to find out how good you are, not how bad you are. They want to get you talking naturally and often find it hard to start the ball rolling. (Some of those interviewing you ask questions merely to show the other members of the committee that they are awake or that they have some special bit of knowledge; so do not look resentful if an occasional rather silly question is asked.)

Some common openings are: "Tell us briefly about your previous experience and education." "Are you interested in any special branch of medicine or surgery?" "What plans have you got for the future and what position do you finally hope to reach?" "What makes you feel that you are a suitable person to fill this post?"

The answers to these questions are often already in front of the board on the copies of the candidate's application, but the board may wish to refresh their memories and usually find the spoken word gives a clearer impression than the written word. It is therefore unwise for a candidate to say "I think you already have those details in front of you." Before the interview it is sensible for a candidate to become clear in his own mind what his interests, ambitions, and capabilities are, so that he can answer the above-mentioned questions. It is unwise to prepare a set speech for an answer, because a prepared reply has a lack of spontaneity which makes it much less compelling than extempore speech.

When speaking at the interview, do not look at the floor or the ceiling, but look one of your interrogators straight in the eye. It is hard for a shy candidate to do this, but he must manage it somehow. It is often difficult to decide which particular member of the interviewing committee to look at. The following suggestions may be helpful. When in doubt address yourself to the chairman. In general look at the person who asked you the question, but if you feel you have focused on one individual too long, turn to the chairman or to the member who seems most interested in what you are saying. If you have had a preliminary interview with a medical selection committee, when you have a second interview with the lay committee address yourself to the lay members of that committee, and avoid unduly technical expressions. Many candidates make a bad impression at an interview because they look unfriendly; in fact they look cross, suspicious, or aggressive. This may be their way of concealing either shyness or nervousness, but committees interpret it sometimes as meaning that the man will be abrupt or intimidating to patients. Hence, be friendly with committees and don't look at them as one looks at an opponent in the boxing-ring.

While you are waiting outside with other applicants for the post, passing those interminable cigarette-smoking moments before you are called, do not discuss

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the post and the impending interview with the other candidates. It will only increase your apprehension and probably convince you that all the others are better than yourself. It is better to be silent or to chatter nervously about general topics.

Lastly, remember that the average committee is a good deal more discerning than you think. There are stories of incompetent candidates bluffing their way into high positions, but they are mostly untrue. Inarticulate and inadequate as a candidate's behaviour at an interview may be, the committee will probably make due allowance for it and form a shrewd idea of the personality and potentialities that lie in the background. PROTEUS.

Disabilities

20. CORONARY THROMBOSIS

IT was on a grey, dull, Sunday morning at 7.30, three years ago, that it hit me; and hitting is not a bad description. I was 48, and in the last twenty years I had not had a single day in bed. Two months before, I had woken early in the morning with pain in the front of the chest, behind the second and third costal cartilages; it lasted about ten minutes. This was something new to me and I consulted one of my local colleagues, a very good doctor. The result of an exhaustive overhaul was completely negative: "Can't find a thing the matter, old boy; probably some indigestion; cut down the smoking," and so on.

In the last five years my job as a G.P. surgeon had not been too easy: the house had a direct hit; the family were evacuated five hundred miles away; the practice had just vanished; and there were lots of worries, financial and domestic. Still, between periods of being frightened to death or bored stiff I had a happy enough time; a long operating session on the ghastly bomb or shell injuries would be followed by a day with the Home Guard, tearing over the downs and initiating them in the use of the Vickers machine-gun. Just my private army. What fun it was and what an antidote.

To revert to that Sunday morning: the pain was severe, very, centring on the middle of the chest over the second and third costal cartilages; it did not radiate down the arms. It was a gnawing, screwing pain—as if someone was applying a vice behind the sternum; and it gradually got worse. I was alone; my general factotum had not yet arrived. I got out of bed and walked up and down, but it was no use; any drugs were downstairs and I could not, or would not, go and get them. "Besides," I thought, "I can do nothing"; and as I had never taken anything except aspirin and alkalis in my life and was going to die in any case, why bother? But I wished it would hurry up; "and why should I go out this way when I missed the bombs and shells in this war and got away with the Salient and the Somme in the last one?" All these thoughts passed through my mind. I hugged the side of the bed, and then I must have passed out, for the next thing I remember was seeing my old factotum with the morning tea. She took one look and grabbed the telephone. My partner arrived and pushed some morphine into me, a big dose. I had never had morphine before—what a joy and relief! In the meantime I had sweated right through a large woollen dressing-gown.

Afterwards I had a vague notion of being trundled down into an ambulance in a canvas carrying stretcher. That evening the nearest consultant, first-class at his job, arrived from twenty miles away and gave the gravest prognosis to my partner: "he will probably be dead by the morning." (I have no doubt that at the time he was perfectly justified; but since then he and I have often laughed about it.) I gathered later that my pulse was all over the place, with a systolic blood-pressure well under 80, and terrific left-ventricle dilation, the apex-beat being somewhere near the backbone. But all the pain had gone and I was comfortable. I had more morphine again that night, for which I was very grateful.

The next day a very distinguished general consulting physician arrived from London (thank God there are still some left); and quite properly, I think, he also took a grave view. I was in no pain but had the most frightful flatulence—fore and aft, chiefly fore. I was nursed sitting up and watched my epigastrium fluttering with sickening cardiac irregularities. Another annoyance was my tongue; it was red and clean from tip to base, but very sore. The pulse was still nobody's business, and an electrocardiogram done that day indicated a large block in the left coronary artery. My memory of the first week is rather vague; I was having morphine and hypnotics at night and digitaline gr. $^1/_{600}$ three times a day. The days passed in a dreamy haze broken only by the confounded flatulence. After using the bedpan twice I flatly refused to have anything more to do with it and insisted on being lifted out and assisted to the commode. This created an uproar, as strict orders had been given that I was not to be moved at all for at least a month. "Well," I said, "if I am going to die I am going to die on the commode and be damned to everyone; don't tell me that there is less cardiac strain on the bedpan—it just isn't true." I got my own way and still lived. One other annoying thing: I had to be catheterised several times because I simply could not urinate lying down. It took me a week to learn the trick, and I advise everyone over 50 to practise it.

I was seven weeks in bed and have nothing but praise for my nurses. It didn't take long to find that the art of nursing is simply knowing how to nurse, not adopting the attitude of a half-qualified doctor. It was the little things that mattered, and in these I was highly served. My appetite was poor but that did not worry me, and I started to smoke cigarettes after the first three weeks. Extrasystoles were a nuisance, and I took rather a morbid interest in the slow rise of my systolic blood-pressure, which gradually crept up to over the 100 mark. I read all the literature of coronary thrombosis I could lay my hands on, from Tom Lewis downwards, and was neither enlightened nor amused. "Heavens," I said, "we know nothing about it apart from post-mortem appearances," and so I turned to P. G. Wodehouse. I got up in the eighth week and went out convalescent in the ninth.

One's mental outlook at this stage seemed completely to overshadow the physical disability. All the gloomy prognostications came to my mind: "Oh yes, old So-and-So had a C.T., you know. He's finished for keeps—such a pity. He was doing first-class work and was just on the top of the wave, and now he's retired to an old lighthouse and just does some quiet prawning," or "he's gone to the Ministry of Pensions." Multiply such statements by ten and that is how one felt.

I found there were three physical disabilities—insomnia, flatulence, and inability to walk any distance without pain in the legs. The first two could be coped with, but the cramp in the calves was an infernal nuisance. It was not a claudication; the pain was centred over the tubercle of the scaphoid of both feet. I simply could not make it out, for my muscles were quite well developed. Curiously enough I had no dyspnœa and no precordial pain, and my extrasystoles had gone; but the pain in the feet and calves went on. I drove the car 200 miles at a sitting without any effort, but as soon as I got out and set my feet to the ground it all started again. This went on for two months without a let-up. I was getting quite worried about it when suddenly on getting out of bed one morning it vanished and has never come back again. That just made all the difference and my remaining month of convalescence was straightforward. During these months I took no drugs except occasionally a mild hypnotic. I carried a 'Tubonic' ampoule of

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morphine with me, and some trinitrin, but I never used either. I also took vitamin B for about six weeks.

I returned to work five months from the day of my attack, and now, two and a half years later, I am working as hard as twenty years ago. I smoke about thirty cigarettes a day, play a round of golf on Sunday, and in summer swim in the sea about once a week. Disabilities? They are these: if I play golf in the wind I get desperately tired; so if there is a very strong breeze I don't play. If the operating-theatre gets very hot I have had enough operating after three hours. Also if I am in a close stuffy room for any time I hate it. Driving the car is not at all tiring; I have driven 300 miles in one day without any ill effect. I have no pain but occasional precordial aches of which I take no notice. A big meal causes more annoyance than anything else, but one occasionally slips up over this. Sleep varies, but I am used to that now. I take no cardiac drugs of any kind but occasionally some vitamin B; whether it does any good I don't know. Flatulence, upwards, is a nuisance at times, but is easily relieved by alkalis.

I am eternally grateful to the consultant who, before I had found my legs again, said "you'll be playing golf again in six months' time." I couldn't believe him; the whole world had tumbled down and I thought I was a permanent crock; but he was right, and he was no cardiologist. My advice to anyone unfortunate enough to get a coronary thrombosis is this: have your cardiologist see you at your initial attack and let him play with his machine and other gadgets, but afterwards see him seldom if at all. If you are willing to be a permanent hypochondriac, well go on seeing him. He will want to go on taking cardiograms and stop you doing all the nice things you want to do.—But if your myocardium is going to let you down with a bump, it will, so why bother?

In general practice, if you tell a patient that he has a bad heart you will kill him dead. People's hearts are everything to them, and if you tell them they are firing on two cylinders, that there is no hope of "decoking," and that their oil pipe is furred up, what on earth do you expect their reaction to be, when they know they can't get a new engine even with priority! I met a young lad the other day—a bright young man—who had just got his M.R.C.P. Said I, "What are you going to do?" "Oh," he said, "I'm going to specialise in hearts." I said, "You go out into general practice for three years first." He said, "Heavens, no! I would be completely out of touch with all the recent advance in cardiology." I wept.

You will have no satisfaction from wading through the present literature on the subject; the age of incidence has come a long way down. One cannot assign the onset to any definite entity. Myself I believe that, far back, coronary thrombosis is of emotional origin—call it psychosomatic if you like. Don't tell me that the higher centres (where are they now?) cannot produce organic changes. They can and do, and I think that if we let our natural emotions and inclinations have a normal outlet, a little more back to the primitive, many such conditions as this would not arise. I have yet to learn of Cabinet Ministers getting C.T.; they seem to go on for ever! Is it that politics desensitise one to the everyday worries?

"Well," you say, "this generalising of yours is all very well, but what is *your* answer to coronary thrombosis?" This is my answer:

> "If on a Spring night I went by
> And God were standing there,
> What is the prayer that I would cry
> To Him? This is the prayer—
> O Lord of courage grave,
> O Master of this night of Spring!
> Make firm in me a *heart* too brave
> To ask Thee anything."
>
> (GALSWORTHY)

In England Now

A Running Commentary by Peripatetic Correspondents

SOMEHOW or other I have never managed to learn about ophthalmology; and I always carry my ophthalmoscope into exams in order to escape the subject—like my aunt Agatha who is convinced that rain never falls so long as she carries her umbrella. You can imagine then how my heart fell into my boots when the Great Man said to me, "Ah! I see you have an ophthalmoscope. If you're interested in eyes you'll find these two cases very satisfactory. I'll be back in ten minutes." I remembered then how I had left my *Atlas of Ophthalmoscopic Appearances* on one side, meaning to have a hasty glance at it before setting out for the hospital; only of course there was not time. But I needn't have worried. No sooner had I started to put my machine together than the first patient leant forward and said, "Ah! I see you have a Keeler—excellent little instrument if you'll excuse me saying so. You'd be surprised what a variety of instruments we see coming here year after year. Evidently you have good taste—which is surprising at your age. What are you? 23 or 24? You know I always like to see you young doctors getting through this exam. It's such an important step in your careers, and it is so pleasant for you to be able to specialise early and marry when you are still young. Now you look at my left eye first. Do you see the disc? I can't tell you what it is but the professor always tells the students that it's like a rabbit's eye. No, it doesn't affect my sight at all. . . .The right eye is not so good, except on the nasal side. Tell me what you think it is and I'll tell you if you are right." Luckily I knew one fact about rabbits' eyes.

The other patient was far more garrulous and didn't stop talking for one moment. "Afternoon doc. How's it going? Press on regardless, eh? You interested in eyes? They all like mine. Take a look. There! Have you ever seen anything like that before? No, I thought not; it's not that common you know. I can't tell you what it is because I don't know what disseminated choroiditis means. Don't speak! I know what you're going to ask me next. They always do. No, I haven't had syphilis myself. It was my father you know. Now I'll tell you what this examiner is going to ask you so that you can be thinking of the reply. He's going to say, 'What else might it be?' Retinitis pigmentosa he wants you to say, and then he's going to ask you what the pigment is. I expect you know the answer to that so I needn't tell you. Of course my eyes can't be cured, and my sight will get gradually worse as the years go by. But I don't mind. A short life and a merry one, eh? Have you heard the one about the actress and the . . . ?" And so on.

I wonder if these two experts are still attending the exam and urging specialists to marry young, or whether the examiners caught them out. Anyway that's how I got through—but I haven't married yet.

* * *

To the unbiased observer the practice of obstetrics must seem a relic of the Middle, or Dark, Ages. Normal delivery, so called, is a travesty of mechanics which has been foisted on the unfortunate female of the species only because its inventor lacked the advantages of a proper medical education. In the pre-Listerian era it was no doubt necessary to make do with the facilities provided by nature, and conduct delivery by pulling or pushing an extremely large object through an extremely small hole, with or without the aid of large iron tongs, and to the considerable detriment of both the hole and the object. But the time for such an indelicate and unscientific antic has surely passed.

Those parts of the feminine anatomy that stand in the path of the human battering-ram which is our firstborn seldom recover from the punishment they receive, and the clinics and operating-theatres are filled with tattered semicontinent victims of outmoded physiology. With grim determination the gynæcologists repair the ravages they have wrought, and were it not for their transparent integrity a cynic might suggest that lacerated perineums, torn cervices (and perhaps cervical carcinoma),

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rectocele, cystocele, prolapse, and fistula are the pieces of silver which obstruct a more rational approach to childbirth.

The orthopædic surgeon, the physiotherapist, and the osteopath derive an appreciable part of their income from the chronic backache which comes of forcibly distracted pelvic joints, and the pædiatrician is harrowed by the mental deficiency and spastic limbs occasionally and not unnaturally resulting from a savage process which squashes the fœtal head out of all semblance to the human shape.

The advent of the National Health Service should be an opportunity for organising obstetrics on a modern and efficient basis, and I hope the Minister will instruct his obstetricians to deliver all British subjects as they would remove any other intra-abdominal tumour—by abdominal section, at a time and place convenient to patient and doctor. I confidently predict that in the curriculum of the future student the practice of obstetrics will be limited to a close study of *Cæsarean Section, Regulations for the Performing of* (H.M. Stationery Office, 9*d*.).

* * *

It is now about 346 years since Hamlet first railed with such elegant bitterness against, inter alia, the law's delay. So far as I know nothing has yet been done about it. My latest experience, trivial as these things go, is—to coin a further phrase—just one more straw laid on the poor camel's back. Working one short, a partner being away on well-earned leave, I was summoned to appear on my (nominal) half-holiday to give evidence in a case in which there was no conflict whatsoever of medical opinion. The facts had already been deposed on oath and were not in dispute. For two hours I sat idle in the court, waiting. At 4 P.M., as I was about to be called, the judge—and who shall blame him?—decided that he would like a cup of tea. The court therefore rose, not for a tea interval merely, but for the day, and the case was adjourned till the morrow. When called at last my evidence, including the time employed in taking the oath and in cross-examination, took perhaps three minutes. Thus, another two half-days of a doctor's time were sacrificed to the convenience of the law. Doubtless the law would argue that the doctor is financially recompensed for his loss of time; but that time belongs properly to his patients.

* * *

Now that reciprocity for the Primary has been established between the English and Australasian Colleges of Surgeons, we candidates who will be facing the visiting examiners from England come February feel unique in that we shall be the last Australians so to be judged. Fellows recently returned from the United Kingdom have been subjected to questions galore to discover some pet theory or foible of those who will soon be with us. Alas, there's none so indifferent to the woes of others as a successful candidate and none so faultless as those who examined him. Perhaps it would be a good idea to send examiners from Australia to England every three years to ensure that our Australian Primary undergoes no inimical mutations and to foster its development in happy symbiosis with its parent.

At this my first attempt, I take consolation in the remark of a candidate who said: "It's a pleasure to be failed by the English examiners—they are so courteous about it all."

* * *

My son is away at a prep. school—a good one I think. One of the reasons for sending him there is that he may learn to express himself in clear unequivocal English. Near the end of last term a postcard arrived from his school, written (I speak from personal knowledge) by a charming assistant mistress. "Bill will arrive at Paddington on Thursday, on the train leaving Blankton at 2 P.M. I suggest that boys should be met on the platform by the engine." What a subject for Emett!

* * *

A patient who was a bit "elevenpence-halfpenny to the shilling," as we say in Yorkshire, greeted me on Christmas morning with: "The complaints of the season to you, Doctor."

Letters to the Editor

SURGICAL EXAMINATIONS

SIR,—Letters have appeared recently about the membership examination of the Royal College of Physicians, but the fellowship of the Royal College of Surgeons seems to have been neglected. This examination is unsatisfactory from several points of view, and serious consideration should be given to revising the whole system of membership and fellowship of an institution held in such very high esteem throughout so much of the world.

The present examination does not differentiate between the good surgeons and the hackers; not even between the outstanding candidate, who may be an atrocious surgeon, and the keen dullard, who may be a very competent surgeon. In the last examination there were about 470 candidates; probably 10% of these were outstanding in every way and passed without any difficulty or question on the part of any examiner: another 10% were so poorly prepared that the examiners unanimously failed them; but the remainder, the majority, were average young doctors bent on becoming surgeons, having varying ability, experience, teaching, interests, and manners. To decide which of them deserved to become fellows, to the exclusion of the others, must have been a superhuman task. More than one examiner has admitted that the examination is "largely a matter of luck"—a shocking admission for those who are deciding the fate and career of young men and ultimately the esteem in which the world will hold their college.

Examiners complain that many candidates come up for the final examination totally inadequately prepared. This is very true, and the reason is that an absurd situation has arisen. In order to get a post with good surgical experience and teaching it is necessary to have a fellowship (and sometimes a mastership as well); in order to get a fellowship or mastership it is necessary to have had a post with good experience and teaching! Hence many young men take the examination in the hope that they will be lucky and thus gain the chance of a good surgical education. Some are. I have known men to have passed at the first attempt, two years after qualification, having spent one year in a surgical unit, who are good at book-learning and regurgitation though very ill-practised with a scalpel; while widely experienced older men—some even established in a specialty, and teaching it well—have been failed. The system, not the examiners, is to blame. At present the examination is too much of a lottery. If the candidate meets an examiner with an approach to the subject with which he is familiar, and is asked about fields in which he has had practical experience, he will pass. If either of these conditions is not fulfilled he will fail.

As an unsuccessful candidate I would like to recommend that the examination be made much more difficult, and that the qualifications necessary to entitle one to sit for the final be raised so that the examiners would know that each candidate has had a thorough surgical training before he is seen. Surgery must be learnt by guided experience. May I, therefore, suggest the following system:

The examination whereby one receives a licence to practise should be called a licentiate, as it is by the College of Physicians.

A membership examination should be introduced incorporating the present "primary" and also some further general surgery and pathology. The object would be to decide which men the college feels are worthy of surgical training and to ensure that all going on to this training have a good theoretical background. This examination could be taken any time after qualifying either by licentiate or a university degree. It should be run on lines similar to the present fellowship, but the examiners would only have to decide which candidates deserved training, and not which were already surgeons.

To qualify for the fellowship the candidate should have received at least five years' practical surgical teaching from a recognised master, the first two years being devoted to general surgery and the last three, if desired, to some special branch of surgery. The examination should be a combina-

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tion of general surgery and the specialty which the candidate chooses to offer; this latter part being conducted by specialists in that field. The candidate's standing with his master should be taken into consideration, and part of the examination should entail performing an operation in the chosen specialty at the hospital of an examiner, assisted by the examiner, and of conducting a ward round for the examiner.

This scheme may seem rather radical at first glance, but I feel that it would serve three important purposes: (1) it would guarantee that all surgeons throughout the country, and those leaving this country after a surgical training here, would be of a more uniformly high standard; (2) it would unify the examination for fellowship by including all the specialties in one examination; and (3) by raising the standard of the fellowship it would maintain and even increase the esteem in which the whole world holds the Royal College of Surgeons of England.

ASPIRING YOUNG SURGEON.

PAROXYSMAL SENSORY ATTACKS

SIR,—Transient attacks of angina pectoris are generally supposed to represent local ischæmic episodes in cases of coronary sclerosis, just as the cramp-like pains of intermittent claudication represent acute local muscular ischæmia connected with arterial stenosis in the extremities. Certain conditions of recurrent abdominal pain have been thought (with some post-mortem evidence) to be due to temporary (possibly angiospastic) ischæmic exacerbations in abdominal arteriosclerosis, and by supposed analogy have been termed "abdominal angina." Is there real evidence that paroxysmal sensory, or partly sensory, attacks connected with cerebral arteriosclerosis can be explained in the same way? Following is an example of the type of case to which I refer:

At the commencement of the second world war an elderly, somewhat florid, English lady, married to a German long resident in England, was startled by the intrusion of a policeman who simply made some inquiries into her ordinary hum-drum everyday existence, of which entertaining her friends to afternoon tea, &c., doubtless constituted a main pleasurable feature. This disagreeable shock horrified her. She commenced to have transient recurrent convulsive attacks (like petit mal) heralded by sensory aura-like symptoms, which latter would sometimes occur without any convulsion. She was unable to describe what she felt; but told me that her sensations in connexion with these attacks were so terrible that she "would not wish my worst enemy to suffer in the same way." The neurologist's diagnosis was that these attacks were connected with cerebral arteriosclerosis. No treatment produced permanent benefit, and she died ultimately in a nursing-home. (No necropsy.)

I would ask: can similar senile transient minor epileptiform attacks, including sensory auræ, be explained as due to cerebral arteriosclerosis in the manner suggested above?

One can also imagine that similar symptoms may occasionally occur in younger individuals, and be due to arterial spasm without any underlying real cerebral arteriosclerosis, just as some attacks of so-called pseudo-angina pectoris may perhaps be due to coronary spasm without coronary sclerosis.

London, W.1. F. PARKES WEBER.

RESPIRATORY OBSTRUCTION DURING ANÆSTHESIA

SIR,—I was very interested to read Dr. Laycock's letter of Dec. 11. The condition that he describes is not at all uncommon. It occurs in patients of all ages, but I think is more frequent in children. I have seen it with all types of inhalation anæsthesia, and rather more frequently in light anæsthesia than deep. It usually lasts 10–30 minutes. It does not always involve the whole of one lung; more commonly it is apparent in the lower lobe. The physical signs are dullness to percussion, limitation of movement, and absent or grossly diminished breath sounds. It sometimes occurs when small amounts of mucus are present, but quite frequently no mucus can be aspirated. The attack can usually be cut short by making the patient cough, or by the administration of carbon dioxide.

I had so often seen the condition pass off spontaneously that at one operation for conservative removal of the breast, under light nitrous-oxide, oxygen, and trichlorethylene anæsthesia, I allowed the patient to be taken back to bed with her reflexes present without taking any steps to remedy this condition, which involved the left lower lobe. She developed a typical atelectasis, with recovery after appropriate treatment.

I suspect that many cases of postoperative atelectasis begin in this way on the table. I agree with Dr. Laycock that the condition is probably due to bronchial spasm.

Colchester. DOUGLAS CLENDON.

REGIONAL REPRESENTATION ON THE JOINT TUBERCULOSIS COUNCIL

SIR,—At a recent meeting of doctors working in tuberculosis in the Liverpool region, it was decided to form a Liverpool Region Tuberculosis Society and to seek representation on the Joint Tuberculosis Council. At a time when the J.T.C. is being consulted about terms and conditions of service for tuberculosis workers, it was felt that it was most important that this body should be fully representative of all regions. This view is held by all the sanatorium superintendents and tuberculosis officers.

The J.T.C. have replied that they cannot consider our application for six months, since regional representation will involve amending their constitution. They have advised the Liverpool region to seek representation through the North-Western Tuberculosis Society. Both representatives from the North-Western Society are from the Manchester region, and cannot be expected to know anything about conditions in this region. Furthermore no change in representation could be obtained in this way until the next annual general meeting in June, by which time it is expected that negotiations will be completed.

Our society therefore wishes to protest strongly against the decision of the J.T.C. to deny representation to the Liverpool region during this critical period, and to point out the unrepresentative nature of the J.T.C. as at present constituted.

WILLIAM D. GRAY
Hon. Secretary, Liverpool Region Tuberculosis Society.

5, Brockholme Road, Mossley Hill, Liverpool, 18.

DIMERCAPROL (BAL) AND ETHYLENE DICHLORIDE POISONING

SIR,—According to the report of the Industrial Health Research Board,[1] ethylene dichloride is used as a solvent in the extraction of fats and oils, in chemical synthesis and in cleaning clothes, as an insecticide and fumigant, as a filling for fire extinguishers, and as a stimulant for sprouting potatoes.

Animal experiments show that ethylene dichloride, which is a volatile liquid, is toxic by inhalation. For example, Heppel and his colleagues [2] have shown that daily exposure for seven hours of mice, rats, rabbits, guineapigs, dogs, and pigs to the vapour in air at a concentration of 1500 p.p.m. resulted in the deaths of the majority of animals of each species within six days.

Since cases of ethylene dichloride poisoning in workers exposed to its fumes have been reported from time to time,[3] attempts have been made to find an antidote to the poison. Heppel and his associates [2] in experiments on animals found that a number of substances, including methionine, cysteine, homocystine, *para*-aminobenzoic acid, aniline, and sulphanilamide, given by mouth to animals before exposure to an atmosphere containing ethylene dichloride vapour, protected them against death. Methionine given to rats after their exposure to a toxic concentration of ethylene dichloride in air did not, however, prevent death.

We should like to report some work which shows that dimercaprol (BAL) protects mice to a significant extent against ethylene dichloride poisoning. Experiments on 61 mice, to which ethylene dichloride was administered subcutaneously in solution in arachis oil, showed the

1. Toxicity of Industrial Solvents. *Rep. industr. Hlth Res. Bd, Lond.* no. 80. H.M. Stationery Office. 1937; p. 161.
2. Heppel, L. A., Neal, P. A., Perrin, T. L., Endicott, K. M., Porterfield, V. T. *J. Pharmacol.* 1945, **84**, 53.
3. Wirtschafter, Z. T., Schwartz, E. D. *J. Industr. Hyg.* 1939, **21**, 126. McNally, W. D., Fostbedt, G. *Industr. Med.* 1941, **10**, 373.

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LD 50 to be 395 mg. per kg. body-weight with a standard error of 21·75. When the same substance was administered in a similar way to a further 40 mice, which were treated subcutaneously at the same time with 60 mg. per kg. of dimercaprol in arachis oil, the LD 50 of ethylene dichloride was 622·5 mg. per kg. with a standard error of 41·6. There seems little doubt from these results that the administration of dimercaprol reduces to a statistically highly significant extent the toxicity of ethylene dichloride. Since dimercaprol is a well-recognised antidote to poisoning due to various substances, it seems to us that these results suggest the possible trial of dimercaprol, should cases of ethylene-dichloride poisoning arise.

It is a pleasure to acknowledge the help of Mr. R. A. Hall and Miss J. Pryke in the animal experiments. We are indebted to the directors of Messrs. Allen & Hanburys Ltd. for permission to publish this note.

H. O. J. COLLIER
Pharmacological Laboratory.
Allen & Hanburys Ltd., Ware, Herts.
M. E. H. FITZGERALD
Organic Chemical Department.

NO ROOM AT THE HOSPITAL

SIR,—May I add one or two points to the list of reasons for the shortage of hospital beds given in your leading article of Dec. 18 ? In geriatric units like those of Dr. Warren and Dr. Cosin it is often difficult to discharge patients who have recovered from their illness, owing to social reasons. Since July 5 chronic-sick beds have been separated from the former public-assistance institutions, making it harder to transfer patients from one to the other. To many elderly folk a bed in hospital means security : the outside world is full of troubles and tribulations. In consequence there are a number of old people in hospital who do not need nursing but who prevent others from getting it. The long-stay annexe is one attempt to cope with this situation. Hostels linked to hospitals are another similar development.

An outpatient clinic for elderly patients, linked to a physiotherapy department, laboratory, and X-ray facilities, can cope with many of the cases which would otherwise need admission to hospital. If this be combined with domiciliary visiting—as in the case of the former distric medical officer—the waiting-list of elderly chronic sick usually diminishes and sometimes fades almost completely away. At least this has been my own experience during the past year.

Purley, Surrey. TREVOR H. HOWELL.

SIR,—Speaking of the thorough treatment practised in certain geriatric units, you say that " lack of trained staff, and building difficulties, make it unlikely that this system will be widely adopted in the very near future." I should like to join issue with you on this statement because I consider that such a system is not only universally possible but is an urgent necessity.

The successes attained by Dr. Marjorie Warren and Dr. Cosin in the treatment of illness in old people are due to a fundamental difference in approach to the problem from the negativistic attitude so commonly encountered. I suggest that there are few " chronic hospitals "—which are predominantly occupied by aged sick—where a rational approach along the lines advocated by Dr. Warren and Dr. Cosin would not considerably improve the condition of patients, with the consequent release of beds. Dr. Cosin's hospital at Orsett is a striking example of how much can be done in not very suitable buildings with the minimum of staff.

Furthermore, one must not overlook the necessity for " the right patient in the right bed " which has been stressed by the B.M.A. committee.[1] A considerable number of the aged sick are accommodated in what were formerly public-assistance institutions, together with a diversity of other types of patient, such as mental defectives, destitute infants, unmarried mothers, and fit old people. It is obviously impossible for any one building to cater efficiently for all these different types of case. For this reason a first essential in providing an efficient service for the aged and chronic sick is reorganisation of the facilities available.

Already in one area the former public-assistance institutions are being developed within the framework of a geriatric service. Thus one institution is functioning as a geriatric unit, to which as far as possible new cases in the area are admitted for treatment ; others function as long-stay annexes, for irremediable cases ; and others as hostels for fit old people. Such an allocation of function allows the development of the individual institution along lines most suitable to the type of case for which it caters. Of course, in order to obviate the necessity for large-scale transfers of patients, and consequent hardship, the change in function must of necessity be gradual ; this can be effected by proper control of admissions, and liaison between the welfare and hospital authorities.

Finally an efficient almoner service for patients and relatives is one of the keys to success. All too frequently one finds that inside the portals of a chronic hospital little attention is paid to the problem of getting the patient out into the world once again.

The sooner the chronic hospitals are reorganised and a more vigorous approach to the treatment of illness in old people adopted, the sooner will the hospital requirements of the elderly sick be met, and incidentally the demands on the beds of acute hospitals reduced. It is possible for these measures to be adopted now. They must not be delayed by the excuse that " lack of trained staff and building difficulties " do not permit. Rather must we contrive that the best use be made of existing resources.

Barncoose Hospital, Redruth, Cornwall. THOMAS S. WILSON
County Geriatrician.

SIR,—Your leading article is most timely, and, in re-emphasising the urgency of this problem, it surely cannot fail to stimulate more constructive efforts to solve the present tragic position of the elderly sick.

Concurrently with the much needed long-term planning for a coördinated geriatric medical service, such as that outlined in the B.M.A. report, The Care and Treatment of the Elderly and Infirm, emergency measures also must be set in train at once. Immediate action is called for to alleviate the distress of those elderly patients already waiting at home for non-existent hospital vacancies.

Since July 5 there has been a spate of requests from general practitioners to the Emergency Bed Service for admission to hospitals of such patients, which has placed upon the service an almost intolerable strain. This practice, moreover, has led to the acceptance by hospital management committees of chronic waiting-lists for patients in their own areas. Let us face facts. These chronic waiting-lists are now meaningless and worse than meaningless. Not only do they result in the impersonal devolution of a responsibility which it should be a matter of personal pride to shoulder locally, but the system also tends to build up in the minds of elderly patients and of their often over-strained relatives hopes of ultimate admission to hospital which are for the most part quite unfounded. The elderly sick must be dealt with by *local* bed bureaux and by local solution.

Is it not more honest and realistic to admit frankly that hardly any of these patients will ever reach a hospital bed ? At present they remain at home, often pathetically neglected. Let us instead leave them at home by design, ensuring that such help as can be given in the home is no longer withheld from them. As they cannot be brought into hospital, the policy ought to be " to bring the hospital to them " and to make available to them as many of those hospital facilities as can, in some degree, be reproduced in their own homes.

In the area of the St. Helier hospital management committee attempts are now being made to set up a " domiciliary inpatient " service and to establish a liaison between the hospital's geriatric department and other bodies, whether statutory or voluntary, not under the control of the regional hospital board.

The linch-pin of such a service is the geriatric social worker, based on the hospital, who with the consent

1. First supplement to the report (1947) of the committee on the care and treatment of the elderly and infirm. *Brit. med. J.* suppl. 1948, ii, 71.

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of the general practitioner (often only too gladly given) visits the homes of elderly patients who cannot be admitted. She assesses the patient's immediate needs, makes a report, arranges transport for outpatient attendances at hospital, and sets in motion the various components of this domiciliary scheme. Her team already includes the services of district nurses, home helps, W.V.S. distributors of hot meals and of "home-bound" occupational therapy, and a Red Cross librarian. It is hoped shortly to arrange laundering facilities and perhaps to organise a rota of patient-watchers from neighbours for those—and they are by no means rarely met with—who are entirely alone in their homes.

The three main props on which the whole scheme rests are:

(1) Transport to and from the hospital for medical investigation, physiotherapy, and other treatments,

(2) "meals on wheels," by which the W.V.S. hope before long to deliver one hot meal a day on five days in the week, and

(3) a laundry service.

For any such scheme to succeed, it is imperative that standing liaison committees should be set up, representative of all the statutory and voluntary bodies concerned in the provision of its various components.

Your inference that part-time nurses in hospitals must feel that "they are the staff" and not merely supernumeraries is very true, and it is sad to reflect that such comment should ever have been merited.

The chronic sick, who are silting-up the beds of our acute hospitals, are only a small part of all those elderly patients, both acute and chronic, who must now remain at home. For the latter much more could be done, and it should be done quickly.

E. B. BROOKE.

St. Helier Hospital, Carshalton, Surrey.

OSTEOPATHY

SIR,—In their anxiety to be fair and avoid prejudice during their visit to the London College of Osteopathy, Mr. Batchelor and Mr. Cohen have created the impression that a significant number of educated surgeons would be prepared to countenance some collaboration with osteopaths if the methods of these practitioners were to be observed at first hand. A similar, and in my view, pernicious tolerance is apparent in your own leader on this topic in the same issue. I wish to contest this attitude in the most vigorous terms before it succeeds in getting hold of the popular imagination.

Mr. Batchelor and Mr. Cohen have omitted to emphasise the two factors which have made it possible for osteopathy to have survived, and even flourished, in the face of rational criticism: firstly the personality of the successful operator, and secondly the absence of a genuine follow-up system for late results.

The astonishing potency of the osteopath's personality (his "integrity," as these writers ingenuously term it) reveals itself in the way Mr. Batchelor and Mr. Cohen have had their surgical judgment shaken though their scientific spirits can be felt in rebellion between each of their conciliatory phrases. And if the convictions of surgeons with twenty years' experience can thus be shaken how easily can the credulous public be cured by quackery! The honest inhabitant of the British Isles stands no chance against the fluent fanatic; the London College of Osteopathy has been to Batchelor and Cohen what Berchtesgaden was to Chamberlain. The absence of a scientific follow-up of long-term results is the whole root and origin of osteopathy. It would be fatal to success to request the patient to attend every three months, as do the orthopædic surgeons, because this would sow the seeds of doubt.

But it is the general conclusion—that osteopathy would be permissible if the practitioner were medically qualified—which reveals to me the power which "integrity" has in dulling the faculty of reason in others. To condone the medically qualified and deprecate the non-medical is pure cant. If a doctor, after years of training in pathology and allied subjects, decides to abandon the scientific method and forget all the facts that its application to medicine has revealed since the days of Harvey and Hunter, then there would seem to be only two explanations for such conduct: either he possesses a paranoid mental state and prefers to follow a systematised delusion rather than rational thought, or he is guilty of wilfully suppressing evidence. The only grace for the osteopath is that he should remain non-medical and therefore unable to be intellectually dishonest.

JOHN CHARNLEY.

Department of Orthopædics, Manchester University.

INDEPENDENCE IN RESEARCH

SIR,—In his letter of Dec. 25 Sir Ernest Graham-Little gives three examples to show how scientific thought was influenced by fascist ideology in Germany. We all know, to our cost, that this was true. But it does not follow that all political interest in science and scientific thought is necessarily bad. The point is that there is and can be no science in the world divorced from politics. The root of the matter is *with which policy science is connected, and whose interests it serves.* Because of this it is of vital importance that scientists should make a careful examination of, and know quite a lot about, contemporary politics, and that from their observations they should decide which policies show the way forward for human society, including themselves, and which policies are trying to drag humanity backwards to ultimate bankruptcy. Those of us who have had a scientific education are tempted to consider ourselves to be "rather above" the apparently pointless arguments of politicians and their respective parties. We also know those who pride themselves on keeping an "open mind" where politics are concerned—minds so far open that everything drops through them. But scientists do not live in a vacuum—they are members of society, and their own interests cannot be artificially separated from the interests of society in general. Scientists either help or hinder the evolution of human society.

I heard the broadcasts of the four scientists to which Graham-Little refers. Three of them put political prejudice before their duty, as scientists, of considering the facts, and spent their time, not in discussion of the scientific problems involved but in political diatribes and ranting accusations against Soviet Russia for which they had not the slightest grounds of proof. Prof. J. B. S. Haldane preferred not to give his final opinion until he had perused the full text of the conference of the Academy of Agricultural Sciences in Moscow, including the criticisms of Lysenko's opponents, of which there were not a few. Graham-Little wrongly diagnoses Haldane's reticence as being due to embarrassment in defending Lysenko. However, Haldane did give a reasoned discussion of the relative effects of heredity and environment, which is more than can be said for the other three.

Huby, near Leeds. P. J. WADDINGTON.

RUSSIA, EUROPE, AND W.H.O.

SIR,—In view of the wide circulation abroad of THE LANCET and the weight which is attached to any statements appearing in it, I am sure you will not mind my drawing your attention to certain statements in your annotation of Dec. 4, which might be misinterpreted, particularly by foreign colleagues.

It is not, perhaps, sufficiently clear to readers abroad that the last two sentences of the first paragraph in regard to the reason for the non-attendance of the U.S.S.R. and Byelorussian members express personal views, presumably those of the writer of the article.

The statement "The Assembly had decided that as the headquarters of W.H.O. are to be in Geneva a regional organisation in the full sense of the constitution will not be necessary for Europe" is incorrect. The Health Assembly at their first session delimited six geographical areas, one of which was the "European Area, comprising the whole of Europe," and resolved "to establish regional organisations in these areas as soon as the consent of a majority of Members situated within such area is obtained." The decision to establish a Special Administrative Office for Europe was directed to the separate and temporary problem of war devastated areas, and was outside the wider problem of a full regional organisation for Europe.

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Finally, the proposal of the delegate from Denmark that the temporary special office should be in Copenhagen was based on his special interest in the B.C.G. campaign. Later he withdrew his proposal spontaneously, and I think the use of the word "stubborn" is therefore unfair.

Ministry of Health, London, S.W.1. MELVILLE MACKENZIE
Member of the W.H.O. Executive Board designated by the United Kingdom.

PENILE CARCINOMA AND CIRCUMCISION

SIR,—In your issue of Dec. 18 Dr. Bab gives a nonsensical version of a passage in a paper by myself by quoting the word "train" as "trail" and omitting a whole line. I cannot follow his argument about "preputial mucus," whatever that is, and vaginal carcinoma. He goes on to state that Jewish women "hardly ever" develop carcinoma of the cervix, but gives no numerical data. A collection of material from the literature on the racial and social incidence of cancer of the uterus, which attempts to deal with some of the questions raised by Dr. Bab, will appear in the forthcoming number of the *British Journal of Cancer*.

Pathological Department, St. Bartholomew's Hospital, London, E.C.1. E. L. KENNAWAY.

THE MALE-TOAD TEST FOR PREGNANCY

SIR,—With reference to Dr. Haines's article of Dec. 11, we should like to remark that it has already been observed that some species of batrachia indigenous to the Old World are as reliable as those found in America for pregnancy diagnosis by Galli Mainini's method.

As we reported to the Asociación de Obstetricia y Ginecologia de Barcelona on Nov. 24, we have been working for several months, in the pharmacology department of this institute, under the direction of Prof. F. G. Valdecasas, with common toads and frogs of the species *Bufo vulgaris*, *B. calamita*, and *Rana esculenta*. Results of our tests, which now number nearly a hundred, have been satisfactory. As was indicated by several speakers at the meeting in November, *R. esculenta* is already in general use here for this purpose.

We notice that there have already been reports on the use in Europe of *R. esculenta* [1] and of the toads *B. vulgaris* and *B. calamita*.[2]

Medical Research Institute, University of Barcelona. J. LAPORTE
E. GENOVER.

PRIMARY CARCINOMA OF THE LIVER

SIR,—I should like to comment on the interesting article of Oct. 2 by Dr. Beynon.

He claims that jaundice and ascites are uncommon in primary carcinoma of the liver. In an account of malignant new growths in Filipino children Stransky and Pecache [3] reported a case in which primary carcinoma of the liver first manifested itself with pronounced ascites, melæna, and hæmatemesis. Eight months later the child was readmitted to hospital with severe obstructive jaundice and metastases to bones and lungs. The diagnosis was established by aspiration biopsy of the primary tumour. The child died at the age of 9 years, and post-mortem examination confirmed the diagnosis.

Stransky and Dauis-Lawas [4] have described a case of primary carcinoma of the liver with insidious onset, in which the mother said that the liver tumour started three years before admission. On admission there was severe obstructive jaundice; aspiration biopsy was done. I have performed aspiration biopsy in several cases of primary carcinoma of the liver in adults. I have observed 3 cases with obstructive jaundice and 2 with ascites. Thus these appear to be not uncommon early symptoms of malignant hepatoma.

Dr. Beynon observes that his patient lived for one year after the diagnosis was established, whereas according to the literature the average life-span after the onset of symptoms is four months. Our first patient lived for nine months after the onset of symptoms, while the second survived for more than six months after the diagnosis was established. In the case of an adult the diagnosis of malignant hepatoma was questioned because the patient survived nine months after aspiration biopsy had confirmed the diagnosis; but the condition did in fact prove to be malignant hepatoma. Metastases to the long bones and even the vertebræ, though not mentioned by Dr. Beynon, are fairly common.

Department of Prediatrics, College of Medicine, University of the Philippines, Manila. EUGENE STRANSKY.

1. Hinglais, H., Hinglais, M. *C.R. Acad. Sci., Paris*, 1948, **226**, 1041. Ferreres, J. A. *Laboratio, Barcelona*, 1948, **5**, 535. Anzueta, P. H. *Ibid*, 1948, **6**, 11.
2. Hinglais, H., Hinglais, M. *C.R. Soc. Biol. Paris*, 1948, **142**, 460.
3. *Ann. Pædiat.* 1946, **166**, 139.
4. *Ann. Pædiat.* 1948, **170**, 131.

YOUNG SPECIALISTS IN SEARCH OF A JOB

SIR,—In your issue of Dec. 11 "Critic" drew attention to the difficulties facing those seeking hospital appointments. To me, as a woman, it seems that the difficulty is twice as great for women as for men.

After qualifying in 1938 I held a long series of hospital posts, which were followed by a period of specialist service in the Forces. Since last May I have applied for ten appointments advertised in your journal. So far I have been short-listed for only one; it was not a hospital post and was confined to women applicants only. If this state of affairs persists much longer any hope of obtaining a clinical appointment in the National Health Service must be given up.

M.D., M.R.C.P.

Public Health

Secrecy in Venereal-disease Treatment

BY the National Health Service (Venereal Diseases) Regulations, 1948, the Minister of Health has reimposed the statutory requirement, originally contained in the Public Health (Venereal Diseases) Regulations, 1916, that information about patients attending venereal-disease treatment centres should be confidential. The 1916 regulations were revoked in consequence of the National Health Service Act. The Ministry explains that this caused some misgiving to the public; the new regulations are made "so that voluntary attendance at treatment centres should not in any degree be discouraged."

Influenza in Italy

The present epidemic of mild influenza in Italy is due, according to the W.H.O. division of epidemiology, to virus B. The disease is characterised by high fever, which persists for 2–3 days; attacks last 4–5 days in all. Fatal pulmonary complications have been observed only among the aged.

The Third Quarter

The following statistics have so far been reported for the quarter ended Sept. 30:

—	Births		Deaths		Infant mortality per 1000 live births
	No.	Annual rate per 1000	No.	Annual rate per 1000	
England and Wales ..	192,073	17·6	101,664	9·3	28*
Scotland ..	24,389	18·7	13,650	10·5	40
Eire	16,410	21·9	7886	10·5	38*

* Lowest rate yet recorded.

In *England and Wales* returns by the Social Survey of Sickness [1] show that out of 2626 men interviewed 1499 reported some illness or injury in May and there were 990 consultations with doctors; out of 3187 women interviewed 2207 reported some illness or injury and there were 1248 consultations with doctors. During the three months April, May, and June illness or injury

1. The Registrar-General's Return for the Quarter ended Sept. 30, 1948. H.M. Stationery Office. Pp. 24. 1s.

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of some kind during a month was reported by 63·9% of all persons interviewed; the average incapacity among all persons interviewed was 0·8 of a day per month. Among housewives 72·0% reported having had some illness or injury during a month, compared with the general level of 63·9%.

Parliament

Safe Milk

IN the House of Lords on Dec. 14 Viscount ADDISON, Lord Privy Seal, in moving the second reading of the Milk (Special Designations) Bill said that in 1943 about 7 million gallons of milk was supplied to the market from tuberculin-tested (T.T.) herds. In five years the figure had gone up to 28 million, but this was still only about 9% of the milk consumed by the public. About 70% of all the milk we consumed was now pasteurised; the balance was supplied as produced.

This Bill was designed to secure that in the places where it was made available the public were assured of completely good milk, free from any risk of contamination. It was sometimes suggested that the Bill might prejudice the improvement of our herds, but he was glad to say that the number of attested herds had been more than doubled during the last four years, and there were now 35,700 in England and Wales, representing between them nearly $1^1/_2$ million cattle.

Legal and technical difficulties had delayed the framing of regulations under the Food and Drugs (Milk and Dairies) Act, 1944, but it was hoped that these would be brought into operation at the same time as this Bill which would afford the Ministry more authority in improving our herds. In the Bill it was suggested that there should be certain designations of milk to be sold: T.T. milk, pasteurised milk, and sterilised milk. In addition, there would be accredited milk. In Scotland, which was rather in advance of England in these matters, the equivalent of accredited milk would be standard milk. Accredited and standard milk were to be kept separate and might be sold in specified areas for five years. At the end of that time it was hoped that the producing herds would have reached a higher standard, but in any case the milk derived from these sources would be either pasteurised or sterilised before it was sold to the public. Where was this to be done? It was useless to make these conditions compulsory unless machinery was available for sterilising and pasteurising. They proposed to begin the scheme in districts of 10,000 population. Before a regulation was made specifying a particular area it would be ascertained that there would be adequate machinery.

Lord WEBB-JOHNSON welcomed the Bill warmly. How could he do otherwise when he had seen the suffering children who had been infected by the bovine bacillus? Surely no-one would wish to wait ten or fifteen years until the herds of the country were cleaned up. Let them go on. Nothing should be allowed to delay an advance which could do something to eradicate this infection.

The Earl of LISTOWEL, Minister of State for Colonial Affairs, said the emphasis in the Bill on pasteurisation did not mean that the Government attached less importance to the other methods set out in the white-paper of 1943. He accepted the principle that the basis of a sound milk policy was a well-bred healthy dairy herd. Discussions with the National Veterinary Medical Association on plans for the eradication of tuberculosis on an area basis would take place soon. But they could not wait until the herds were cleaned up before liquid milk for human consumption was rendered safe to the public health. Prompt action was demanded.

Specialists in the Forces

Speaking in the House of Lords on Dec. 14 at the third reading of the National Service (Amendment) Bill Lord WEBB-JOHNSON agreed that experience had shown it to be necessary to extend the calling-up age for medical men and dentists to 30, as otherwise many men would escape liability for service. Medical men were in a special category, as they were called up to commissioned rank; but this was not entirely disinterestedness on the part of the Legislature, for the Services must have medical officers. The deficiency in their numbers was obvious in peace-time, while a deficiency of other experts might only be revealed by war. But he warned their Lordships that raising the age to 30 might not provide the number of general duty medical officers required, because so many ex-Servicemen were going though the medical curriculum at present that the output of men liable for military service might be considerably less than in the past. He feared a shortage of general-duty officers; in fact there was already a shortage of specialists. In the view of the Army Medical Advisory Board, of which he was chairman, and the Medical Personnel Priority Committee, of which he was vice-chairman, specialists could not be provided under the present law. Lord Webb-Johnson therefore urged the Government to improve the terms and conditions of service in the medical branches of the Forces and to work out a scheme whereby the National Health Service could be integrated with the Forces. There would, for instance, he imagined, be a great many specialists holding whole-time appointments. Might not some of these posts carry the obligation to be prepared to be seconded for service with the Forces, the specialist later resuming his old position without losing seniority, his chance of promotion, or other advantage?

QUESTION TIME

Army Nursing Services

Replying to a question, Mr. EMANUEL SHINWELL stated that the King had intimated that as soon as the Army and Air Force (Women's Service) Act has been brought into operation, he will be pleased to constitute the existing Army nursing services—namely, the Queen Alexandra's Imperial Military Nursing Service and its Reserve, and the Territorial Army Nursing Service—a Corps of the Army, with the title Queen Alexandra's Royal Army Nursing Corps.

Body-weight Survey

Sir WILLIAM DARLING asked the Minister of Food what was the name of the agency which is conducting his body-weight survey; when last a survey was made in Scotland; and at what places.—Mr. JOHN STRACHEY replied: The body-weight survey is conducted by Social Surveys Ltd., Aldwych House, London, W.C.2. The last survey in Scotland was made during October and November, 1948, at Aberdeen, Dundee, Dumfermline, Edinburgh, Glasgow, Greenock, Inverness, Johnstone, Kirkcaldy, Paisley, and Perth.

Accommodation for Aged

Mr. F. W. SKINNARD asked the Minister of Health how many infirm aged people in England and Wales were listed by the various county welfare departments as awaiting admission to institutions; and what steps were being taken to provide additional accommodation for such cases.—Mr. ANEURIN BEVAN replied: Numbers are not at present available but I have asked local authorities to include them in the schemes which they are now preparing under the National Assistance Act and which will contain their plans for providing additional accommodation.

Sanatorium Beds

Mr. WILLIAM SHEPHERD asked the Minister what percentage of beds was vacant in tuberculosis sanatoria through lack of nurses.—Mr. BEVAN replied: Eighteen per cent.

Care of the Totally Disabled

Mr. A. R. W. Low asked the Minister of Pensions how many totally incapacitated ex-Servicemen residing in their own homes were in receipt of pensions and allowances of £6 11*s.* per week; and how many of these men had been issued with a car by the Ministry of Pensions.—Mr. H. A. MARQUAND replied: Of those pensioners listed as being in receipt of 100% pension plus the unemployability supplement, 577 are receiving £6 11*s.* per week or more by reason of a higher scale of pension or additional family allowances, but the precise number cannot be stated without examination of a very large number of documents. The distribution of free motor-cars to the seriously disabled is only just beginning. Many of the 577 pensioners referred to are in the classes eligible for a motor-car and they will receive a car in due course. Over a period of two years 1500 cars will be provided.

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Obituary

LIONEL COLLEDGE

M.B. CAMB., F.R.C.S.

Mr. Lionel Colledge, who died in London on Dec. 19, was consulting surgeon to St. George's Hospital and the Royal National Throat, Nose, and Ear Hospital. He was chiefly interested in the surgery of the larynx, and did perhaps more than anyone else to make this a part of regular surgical practice.

Colledge was born, in 1883, at Cheltenham, and he received his early education at Cheltenham College. He went on to Caius College, Cambridge, and then to St. George's Hospital, qualifying M.R.C.S. in 1908. Two years later he graduated M.B., and in 1911 gained the fellowship of the Royal College of Surgeons. After holding junior posts at both hospitals, he was appointed to the honorary staffs of St. George's and the Throat Hospital (as it was then called) in Golden Square.

In the 1914–18 war he served with the R.A.M.C. as aural surgeon to the 1st Army in France, and was mentioned in despatches. He was Semon lecturer at the University of London in 1925, and he served as president of the sections of laryngology and otology of the Royal Society of Medicine. During the inter-war years he extended his hospital activities by taking appointments at the Freemasons' Hospital, the Prince of Wales's Hospital, Tottenham, and the West End Hospital for Nervous Diseases. Shortly before the late war he retired from St. George's, but during the war he took further posts, including one at the Royal Cancer Hospital. He was also consulting aurist to the Royal Navy.

A prolific and able writer, he contributed sections on his specialty to several books. Much of his most important work—on the treatment of laryngeal and facial nerve paralysis—was done jointly with Sir Charles Ballance; and together they published a work on the surgical treatment of paralysis of the vocal chords. He was later associated with Sir StClair Thomson in studies on cancer of the larynx. Eighteen months ago ill health compelled him to give up his hospital posts, with their demands on him as an operating surgeon. He continued, however, in consulting practice.

M. E. writes: "When I heard, some eighteen months ago, of the sudden illness of Lionel Colledge, it seemed quite impossible to believe that that burly and active figure was lying unconscious and desperately ill. It was characteristic of him that he later fought his way back to some semblance of normal life, refusing to admit or even recognise that he had in any way been disabled. 'Lionel' had been so long in the van of laryngology and otology, and was so typical a figure of a bygone day of consulting surgery, that it was difficult to believe that he was by no means an old man. His energy and character had undoubtedly stamped him early in life as a leader, and he must naturally have assumed this position when most men of his age were still struggling for a foothold.

"His special interest was the surgery of cancer in the larynx and pharynx, but his earlier work on facial-nerve anastomosis is apt to be forgotten. He was perhaps not rated especially high as an otologist, but his house-surgeons would say that his mastoidectomies did as well as anyone's, and better than most; he was in fact an outstandingly good mastoid surgeon. Apart from rare, and always brief, shooting holidays he seemed to have few interests outside his work; for relaxation he would read some obscure paper on cancer of the larynx. This absence of outside resources made his last illness especially irksome.

"Like all single-minded men he had dogmatic opinions, and he was impatient of other ideas and not very receptive of them. Thus he was not an easy man to work with unless approached with sympathy for his outlook and understanding of his singleness of purpose and his integrity. Since he never wore his heart on his sleeve, others found it hard to know whether he liked them or not. Punctilious in his work, he was hardly ever late for outpatients or operating, and however large the clinic he was there to the end. 'Lionel' was a personality of mark, and his passing has left a great gap."

Mr. Colledge is survived by his widow and by a daughter, Miss Cecilia Colledge. His only son, who joined the R.A.F. in the late war, was reported missing from operations over Germany in 1943.

ELSIE JEAN DALYELL

O.B.E., M.B. SYDNEY

THE news of the death of Dr. Dalyell on Nov. 1 in Sydney has been received with sorrow by her friends and colleagues in this country.

Born in Australia of Scottish stock, Dr. Dalyell was educated in Sydney and took her medical qualification in 1909. Three years later she came to this country with a Beit fellowship, which she held at the Lister Institute while investigating the intestinal flora of infants. On the outbreak of the 1914–18 war she was released from her fellowship to join the staff of Lady Paget's Hospital at Skoplje in Serbia, where, in collaboration with the late Prof. Hans Zinsser, of Harvard, and in almost impossible conditions, she helped in the fight against the great typhus epidemic of 1915. Her war service was continued from 1917 to 1919 in the Royal Army Medical Corps, in which she served as pathologist in Malta, Salonika, and Constantinople.

The autumn of 1919 found Dr. Dalyell in Vienna, where for the next three years she worked as senior clinician with the small band of women who, on behalf of the Lister Institute and Medical Research Council, studied the nutritional diseases seen in Austria after the deprivation of the war. The task of this small mission, some of whose members had been engaged in experimental work on the cure and prevention of deficiency diseases in animals, was to convey experimental results to the Viennese medical profession, and to ascertain how far these were applicable to human beings. Their investigations into the ætiology of rickets, with the coöperation of the late Professor von Pirquet and his staff at the University Kinderklinik, were a substantial contribution to our knowledge of the causes of this disorder, which at that time were obscure and the subject of some rather heated controversies, long since reconciled.

After her return to Australia in 1923 Dr. Dalyell joined the staff of the New South Wales public-health department as officer in charge of the serological section—a position she held until 1945. During her period of office, she found time for many outside activities, including the development of the venereal-diseases clinic at the Rachel Forster Hospital for Women, where, in accordance with her firm conviction, the closest collaboration was maintained between laboratory investigation and the clinical diagnosis and treatment of the patient. During the 1939–45 war much of her small leisure was devoted to work for the local blood-transfusion service, which, together with part-time work as pathologist at two country hospitals, she continued after her formal retirement from the public-health service.

"Of late one of her greatest satisfactions," writes an English colleague, "was in sending food to her friends in this country, who received a ceaseless flow of parcels containing items well chosen to supply existing deficiencies and to provide welcome luxuries. For the last year of her life she had carried on with courage in spite of a serious heart condition, the result in part at least of the strain and overwork of the war years. An adventurous spirit and a lovable nature, in her vivid personality the most generous impulses were combined with a great capacity for hard work. She will be greatly missed, not only in her own Australian circle, but also by her friends in this country to whom she had promised a visit, and who had never given up the hope of seeing her again after so long."

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Notes and News

UNIVERSITY GRANTS COMMITTEE

THE term of office of a number of members is about to expire and this committee has been reconstituted with the following members: Sir Walter Moberly (chairman), Mr. A. E. Trueman (deputy chairman), Prof. E. D. Adrian, O.M., F.R.C.P., Sir Charles Darwin, Miss D. Dymond, Mr. H. L. Elvin, Mr. E. James, Mr. H. S. Magnay, Prof. W. R. Niblett, Prof. P. S. Noble, Prof. D. Hughes Parry, Prof. G. W. Pickering, F.R.C.P., Prof. E. K. Rideal, Prof. H. G. Sanders, Prof. J. C. Spence, F.R.C.P., Sir Alexander Stephen, Mr. B. H. Sumner, and Miss Barbara Wootton.

SCOTTISH APPOINTMENTS SCHEME

To help doctors in Scotland who are seeking medical appointments outside general practice, the Ministry of Labour's appointments service in Scotland is maintaining at the Edinburgh office, 5, Rothesay Terrace, and at the Glasgow office, 450, Sauchiehall Street, registers of doctors and of appointments open to them. This means that information about appointments with hospital boards, boards of management, local authorities, &c. can be obtained from the offices. The department has the coöperation of the Scottish committee of the British Medical Association, which is consulted on all matters concerning remuneration, and of the Department of Health for Scotland, and has the help of a medical member of its own staff as technical adviser. Openings in general practice are covered by the Edinburgh office of the association's Medical Practices Advisory Bureau, 7, Drumsheugh Gardens, and it has been agreed that should the bureau later expand its operation to cover any group of appointments now dealt with by the Ministry's Appointments Service, this section of the scheme will be handed over to the bureau.

RESEARCH IN CHILD DEVELOPMENT

IN 1947 Prof. Alan Moncrieff, of the Institute of Child Health, and Dr. D. H. Geffen, medical officer of health of St. Pancras, suggested to the governors of the Foundling Hospital that research and teaching should be arranged in the hospital's residential and day nursery, and nursery school at Coram Gardens. They also suggested that a maternity and child-welfare centre might be started on the same site by reconstructing a derelict building. Meanwhile the Central Council for Training in Child Care, who under the Children Act train boarding-out officers and house mothers, had asked for help in training supervisors and tutors for their education schemes. The governors were favourable, and it was finally agreed that the Institute of Education of London University should finance the teaching side of the new project, and share with the Institute of Child Health in financing the research side.

The first training course will begin this month. Dr. Agatha Bowley has been appointed senior lecturer in child care, with Miss J. E. Cass as tutor; the teaching staff of both institutes will take part in the course. Miss Cass has also been appointed honorary educational supervisor of the day nursery. The child-guidance clinic of Great Ormond Street Hospital is giving help on the research side, and a part-time medical assistant and two assistants in educational research have been appointed. Studies are to be made of the children in the nurseries and nursery school, and if possible of babies and young children in the area who are not attending such centres. A pilot survey is already planned, and it is hoped that ultimately it will be possible to evaluate the advantages and drawbacks of nurseries and nursery schools. It should also be possible to follow some of the children through their primary-school life and even on to adolescence, when they may be expected to join the youth centre in the Harmsworth Memorial Playground, also on the Foundling site. Such long-term surveys have hardly been made before in this country, and should yield valuable information.

International Congress of Psychiatry

An international congress of psychiatry will be held in Paris from Oct. 4 to 12, 1950. The British committee includes: Dr. J. R. Rees (chairman), Dr. T. P. Rees, Dr. G. B. James, Dr. W. S. Maclay, Dr. R. Ström-Olsen, Dr. L. C. Cook, and Mr. Geoffrey Edwards (secretary). The secretary-general of the congress is Dr. Henri Ey, 1, rue Cabanais, Paris, XIV.

University of Cambridge

On Dec. 11 the following degrees were conferred:

M.B., B.Chir.—Camilla B. P. Bosanquet,* Pamela E. Davis, H. L. J. Wilson.*

* By proxy.

University of London

The title of professor of pathology has been conferred on Dr. H. W. C. Vines, and the title of professor of chemical pathology on Mr. Jocelyn Patterson, PH.D., in respect of the posts held by them at Charing Cross Hospital medical school.

On Wednesday, Jan. 12, at 5.30 P.M. Prof. G. Toverud, director of the department of pedodontia in the dental school, Oslo, will give a lecture at the Senate House, Russell Square, W.C.1. He is to speak on the Influence of General Health Supervision on the Frequency of Dental Caries in Norwegian Children.

At a recent examination for the D.M.R. H. F. T. Deane was successful.

University of Manchester

At recent examinations the following were successful:

M.B., Ch.B.—Margaret Armitstead, Mary P. Armstrong, J. M. Bernstein, P. H. Bracewell, Vernon Broadhurst, R. B. Charnock, Montague Cohen, J. L. Cotton, Brian Gill, Doreen M. Ginever, Barbara Hall, Bernard Hendy, Muriel M. Hughes, Harry McIntyre, C. A. Mavs, Kenneth Rawnsley, W. R. Riley, Beatrice E. Sleigh, R. V. Sykes, Ruth Tattersall, D. B. S. Taylor, I. G. Taylor, Helen L. S. Tennent, J. B. D. Torr, J. D. Villiers, J. M. Watt, H. L. Wayne, Doreen Wilkinson.

D.P.M. (part II).—Erich Gostynski, H. F. Jarvie.

Mr. W. F. Nicholson has been appointed lecturer in surgery.

University of Liverpool

At recent examinations the following were successful:

M.D.—C. D. Alergant, H. Angelman, H. B. N. Jennings, J. Mills, R. H. M. Stewart, R. H. White-Jones, F. J. Zacharias.

M.Ch.Orth.—G. W. Baker, R. F. Browne, N. A. G. Covell, R. H. Dawson, T. Denness, P. K. Duraiswami, M. J. Gallagher, J. R. Hughes, W. A. Hugh-Smith, A. F. McSweeny, A. B. D. Minnaar, L. Mirkin, B. Mukopadhaya, R. F. O'Driscoll, W. H. G. Patton, J. H. G. Robertson, A. K. Saha, G. L. Shatwell, C. C. Slack, E. A. Smyth, I. D. Sutherland, W. J. Virgin.

M.B., Ch.B. (part III, old regulations).—C. E. Arkle, N. O. Ascroft, G. Bilsbarrow, J. D. E. Edwards, Elspeth M. Evans, J. A. Finnigan, Gwen E. Hughes, T. J. M. Hughes, Gwenyth H. Kendrick, J. H. Murray, N. C. W. Owen, W. H. Parry, Enid Rees, Joyce L. Rowley.

University of Durham

On Dec. 17 the following degrees were conferred:

M.B., B.S.—G. L. Anderson, Anne R. Boon, P. G. Buck, Maureen T. Cunningham, June Dickson, Irene N. Dodd, Mildred C. Gardner, Sheila L. Harrison, Elizabeth J. Hunter, Alix P. M. Hurst, Eileen Hutton, Hazel E. Jopling, R. N. C. Lockey, Joseph McManners, J. G. Noble, Edith M. Robertson, Donald Smith, J. D. R. Smith, Joan Stephens, A. E. Wright.

University of Leeds

Dr. T. D. Day has been appointed a senior research fellow in experimental pathology and cancer research.

University of Edinburgh

On Dec. 17, the following degrees and diplomas were conferred:

M.D.—J. M. Alston (awarded medal); W. J. Matheson, Helen R. Neve.

M.Ch.—E. A. Jack (highly commended).

Ph.D. (in the faculty of medicine).—I. F. Sommerville, Abraham Stolman.*

M.B., Ch.B.—Dores Baxter, Harold Cameron, Isabel A. Cossar, Jack Darnborough, J. C. Edie, W. D. Elliott, A. C. Ferguson, I. G. P. Fraser, G. B. Goodman, Alexander Gordon, P. F. Green, D. H. Haworth, S. P. A. Henderson, J. W. Herries, C. F. Hogg, J. T. Lamb, M. H. Lawrence, A. C. MacRae, Ann H. Miller, M. M. Milne, P. A. Moffat, Agnes C. D. Penman, T. R. Preston, M. L. Roden, B. H. Shiel, Catherine B. G. Sinclair, D. M. W. Smith, C. C. R. Walker, D. C. M. Wilcox.

D.T.M. & H.—S. R. A. Messih.*

D.M.R.D.—L. D. Keegan,* L. D. Philp,* P. St. G. Robinson.*

D.M.R.T.—J. A. Caskey,* W. B. Dawson,* Mary A. J. T. Douglas,* J. F. Riley.*

M.B., Ch.B. of the Polish School of Medicine.—Jewel Ajzenberg, Bolesław Barczynski, Witold Browarski,* Paulina M. Cieńska, Stefania Cywińska,* Józef Dabrowski, Elżbieta A. De Costres, Franciszek Dulian, Franciszek Fundament, Krystyna M. Gottlieb, Maria Hlawiczka, Tessa Holcman, Lucjan Krȩcki, Jan Lacny, Krystyna Lourie, Halina B. Marszalek, Szabsa Markus,* T. M. Nowosielski, Roman Starczewski, Eugeniusz Szlamp, Irena Weissman,* Antoni Wittek,* Ludmila Zaleska,* Bożena Ziolkowska.

* In absentia.

The Chadwick medal in sanitary science was awarded to Dr. G. O. Mayne.

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University of Bristol

At recent examinations the following were successful:

M.B., Ch.B.—R. J. Carey, Anne B. Cousins, Vera H. M. Dowling, D. N. Fitzgerald, Margaret Ford, Anne M. French, B. T. Hale, G. A. Hanks, Kathleen J. Harrison, Joan A. Higginbottom, Una P. Jones, A. H. Laxton, A. J. Lee, D. B. Peacock, Elizabeth Preston-Thomas, G. T. Salter, P. J. Speller, Maro A. Wells; *in group I (completing examination)* G. D. Teague, A. S. Wallace; *in group II (completing examination)* Pamela L. C. Watson.

D.P.M. (part II).—M. A. X. Cocheme, V. G. Crotty, W. A. Heaton-Ward.

D.M.R.D. (part II).—D. M. P. R. Clarke.

Royal College of Surgeons of Edinburgh

At a meeting of the college held on Dec. 15, with Mr. Frank Jardine, the president, in the chair, the following were admitted to the fellowship:

Tariq Munir Abbas, Solomon Abel, A. F. Alexander, P. St. G. Anderson, R. W. Baillie, J. A. Barclay, A. E. Bateman, H. A. Benjamin, Constance L. Beynon, Satya Charan Bhattacharyya, H. G. Biggart, H. D. W. Black, J. S. Boyd, Ivan Bruce, Alexander Buchan, George Buchanan, J. S. Calnan, J. D. Cameron, J. A. Campbell, N. A. Campbell, J. S. Cason, Zinnur Ahmed Choudhuri, K. S. Clarke, K. W. Cochrane, R. B. G. Cook, J. W. Cowie, C. S. Dafoe, K. H. Dalrymple, W. J. Dempster, W. R. Dickie, C. A. P. Donaldson, A. G. Gibb, C. A. Gleadhill, A. G. Gray, L. M. Green, W. S. Hanna, Phillip Harris, A. R. Harper, C. J. Hassett, J. R. Hochhauser, V. S. Hughes-Davies, R. F. Jackson, E. W. Jeyaratnam, Arthur Joffe, A. M. Keith, J. R. Kenyon, D. R. Kilgour, Shreedhar Shreenivas Kirtane, A. P. Kitchin, J. W. Knox, Tecklim Koonvisal, D. W. Lamb, A. S. Lewis, R. A. Lindsay, Ursula M. Lister, H. K. Lucas, J. T. Mair, Rabindra Nath Guha Majumder, T. S. Matheson, A. J. M. Mathieson, A. B. May, Ramchand Kishindas Menda, I. H. Meyer, A. M. Michael, J. P. Mitchell, Robert Morrison, John Mowat, A. A. Murray, J. H. McBeath, R. J. M. McCormack, A. B. McCulloch, D. M. Macdonald, G. H. D. McNaught, C. G. Nairn, J. G. Napier, E. L. Nicolson, T. H. Norton, W. D. Paterson, B. H. Price, Ghias-Ud-Din Qazi, P. T. Quinlan, Mohammed Siddique Qureshi, Florence C. R. Richardson, E. F. Ridley, L. R. Robson, P. E. Roland, Norman Rosenzweig, Abdel Megid Sadek, Himadri Kumar Sarkar, A. S. Scott, L. S. Scott, R. H. Sewell, Shrikrishna, J. J. Skapinker, A. D. Smit, P. H. E. Smith, E. F. G. Stewart, B. A. Thompson, G. R. Thomson, Norman Tunnell, P. R. Walbaum, R. B. Watson, Catrin M. Williams, R. G. Williams, Eileen D. M. Wilson, David Wright, J. H. Wrigley, Sidney Zinn.

Royal Faculty of Physicians and Surgeons of Glasgow

Dr. H. C. Cameron will deliver the Dr. John Burns lecture to the faculty at 242, St. Vincent Street, Glasgow, on Wednesday, Jan. 12, at 5 P.M. He is to speak on the Beginnings of Modern Surgery, with personal recollections of Lord Lister.

Faculty of Homœopathy

At a meeting of the faculty to be held at the Royal London Homœopathic Hospital, on Thursday, Jan. 6, at 5 P.M., Dr. W. Lees Templeton and Dr. Charles Kennedy will read a paper on Head Hunters in Great Ormond Street.

Hadassah Medical Organisation

Dr. Eli Davis has been appointed director of the organisation. Dr. Davis was formerly deputy medical superintendent of St. Andrews Hospital (L.C.C.).

Royal Institution

Sir Frederic Bartlett, F.R.S., is giving a course of Christmas lectures at the institution, 21, Albemarle Street, London, W.1, on the Mind at Work and Play. The concluding lectures in the series will be held on Jan. 4, 6, and 8 at 3 P.M.

Wellcome Historical Medical Museum

Exhibitions on the History of the Microscope in relation to Medicine, and on the History of Surgery are now being held at the museum, 28, Portman Square, London, W.1. They will be open daily (except Sundays) from 10 A.M. to 5 P.M. for a limited period. Admission is free.

B.M.A. Libel Actions

On Dec. 21 a statement was read before Mr. Justice Hilbery in the High Court on behalf of Daily Mirror Newspapers Ltd., defendants in an action brought by the British Medical Association, disclaiming their intention to impugn the honesty of the association in connexion with the ballot on the National Health Service. As a token of good faith they agreed to pay a substantial sum to a medical charity and to indemnify the association against costs. A similar declaration was read on behalf of Dr. S. W. Jeger, Mr. Somerville Hastings, Dr. Louis Comyns, and Dr. H. W. B. Morgan, defendants in a second action. Mr. Justice Hilbery directed that the record in each action should be withdrawn.

London School of Hygiene and Tropical Medicine

The Langley prize, which is open to competition among officers, past and present, of the West African medical departments, has been awarded to Dr. Fitzgerald Moore for his essay on Nutritional Eye Disease and Effects of Nutritional Retrobulbar Neuritis.

Royal Society

Dr. Robert Barer has been appointed Alan Johnston Lawrence and Moseley research fellow of the society for two years, renewable for a further three years. He will continue his work in the department of human anatomy at Oxford on the biological and medical applications of new methods of microscopy, with special reference to the Burch reflecting microscope.

Dr. S. Leonard Simpson has been elected an honorary corresponding member of the French Society of Endocrinology.

CORRIGENDUM.—*Surface-active Compounds in the Chemotherapy of Tuberculosis:* In the last paragraph of this annotation last week the suggestion intended was that if *in-vivo* testing shows enhanced tuberculostatic activity, such drugs as streptomycin and *p*-aminobenzoic acid should be rendered surface-active.

Diary of the Week

JAN. 2 TO 8

Tuesday, 4th

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. M. Sydney Thomson: Zoonoses (Parasitic Infections).

Thursday, 6th

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park, S.W.1
4.30 P.M. Lecture demonstration on psychiatry.
INSTITUTE OF DERMATOLOGY
5 P.M. Dr. G. B. Dowling: Cutaneous Tuberculosis.

Friday, 7th

MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, W.9
5 P.M. Dr. Douglas McAlpine: Case demonstration.

Appointments

ALLISON, V. D., M.D. Belf., D.P.H.: director of laboratory services for the Northern Ireland Hospitals Authority, Belfast.

Royal Hospital, Mosul, Iraq:

BARSBY, BERYL, M.D. Lond., M.R.C.P.: specialist in internal diseases.
SMITH, B. W., M.B. Lond., F.R.C.S.: specialist surgeon.

Births, Marriages, and Deaths

BIRTHS

BOWEN-DAVIES.—On Dec. 19, in London, the wife of Mr. A. Bowen-Davies, F.R.C.S.—a son.
COOPER.—On Dec. 18, the wife of Dr. Peter Cooper—twin sons.
EWING.—On Dec. 18, in Surrey, the wife of Mr. Maurice R. Ewing, F.R.C.S.—a son.
GOODHART.—On Dec. 15, at Bromley, Kent, the wife of Dr. John Goodhart—a son.
MACKEITH.—On Dec. 13, in London, the wife of Dr. Ronald MacKeith—a daughter.
MARTEN.—On Dec. 1, in London, the wife of Dr. Robert Marten—a son.
NEVILLE-SMITH.—On Dec. 21, at Marlborough, the wife of Dr. C. H. Neville-Smith—a son.
PARKER.—On Dec. 15, the wife of Mr. Geoffroy Parker, D.S.O., F.R.C.S.—a son.

MARRIAGES

FAULKNER—GEARY.—On Dec. 11, in London, Thomas Faulkner F.R.C.S., to Felicity Geary.
GILFORD—GOWANS.—On Dec. 18, at Tonbridge, Walter W. Gilford, F.R.C.S., to Edith Gowans.
LEON—WARD.—On Dec. 16, in London, Kenneth Wilfred Leon, M.R.C.S., to Mrs. Patricia Ward.
MARTIN—WORTH.—On Dec. 22, in London, Nicholas H. Martin, M.R.C.P., to Ursula Worth.

DEATHS

BUNTING.—On Dec. 15, William Hartley Bunting, M.D. Edin., F.R.C.S.E., aged 80.
COLLEDGE.—On Dec. 19, in London, Lionel Colledge, M.B. Camb., F.R.C.S.
MORLAND.—On Dec. 21, Mary Windsor Morland, aged 75, wife of Dr. Egbert Morland, of Pell Croft, Wooldale, Holmfirth, Yorks.
MORRISON.—On Dec. 17, at North Walsham, Norfolk, Henry Morrison, M.A., M.D. Camb., aged 54.

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HISTORICAL BUILDING
DES MOINES, IOWA

DANGERS OF CRIMINAL INSTRUMENTAL ABORTION *

KEITH SIMPSON
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SOME 110,000–150,000 abortions take place every year in England and Wales (Interdepartmental Committee on Abortion 1939), and probably at least 40% of these are induced unlawfully and without proper medical indication. The incidence is difficult to assess owing to the natural reticence of both women and doctors to report such matters when they have no duty to do so and can see no advantage in it; but, if this conservative figure is accepted, it follows that there are 300–400 criminal abortions in England and Wales *every day*.

Apart from the substantial loss to the population, there is far more grave and lasting harm to fertile women. The premature termination of a pregnancy can cause infinitely more lasting harm than can birth at, or near, term, for it takes place without the advantage of choice of place or time and it lacks skilled attention, surgical cleanliness, and aftercare. Only too often it is casual or planned for mere domestic or social convenience, and carried out in secrecy, for gain, by persons uninterested in the ultimate health of the wretched subject.

The two main classes of criminal instrumental abortion are:

(1) *Domestic*, often self-procured, or at best with the assistance (encouragement would be a more appropriate word) of the mother or some other older women—clumsy, unskilled, blunderingly dangerous, and dirty.

(2) By *habitual abortionists*—by persons with varying knowledge, skill, and care, from lower-class women earning £2–5 a time, to doctors in practice earning what they can before the law overtakes them.

The dangers are more serious where there is no trained skill and no knowledge of the need for delicacy and surgical cleanliness. Only the chemist, the doctor, and the midwife who have descended to these practices come near to escaping danger owing to their training. The others are attended by an almost unlimited variety of complications, of which some, such as shock and air embolism, develop before the woman can be got off the premises, and others, such as septicæmia and nephritis, may develop insidiously over days or weeks and last indefinitely.

The mortality appears surprisingly low—no more than 0·3–0·4% or so deaths from causes connected directly or indirectly with abortion. A mere 500 or so deaths from these causes appear annually in the Registrar-General's returns for deaths in England and Wales. This is no true reflection of the actual incidence. The figure gives no indication of the ill health and sterility which result from procured abortion. Though the mortality may be low, the morbidity is very high indeed.

Both of the common forms of criminal interference with a pregnancy—by drugs and by instruments—have their peculiar complications, but the dangers of abortifacient drugs are trivialities of toxicology only. The Interdepartmental Committee on Abortion (1939) made it clear that the use of drugs was far more likely to cause misery and serious toxic symptoms than to promote abortion:

> "Although in certain circumstances these preparations may bring about termination of pregnancy, the primary evils arising from their sale, as we see them, are the fraudulent exploitation of the mental distress of the women who buy them in the anticipation that they will cause abortion; and the danger to health, and, at times, to life which attends their indiscriminate use."

* Based on a lecture at the Royal College of Surgeons on Sept. 5, 1947.

FORMS OF INSTRUMENTAL ABORTION

The forms of instrument in use for the dislodgment of a pregnancy are legion, for a pregnant woman in a state of anxiety will use anything from a crochet-hook to the most complicated system of irrigating apparatus in order to rid herself of an unwanted child. The purpose of instrumentation is either to dilate the cervix so that the uterus will contract reflexly and empty itself, or to penetrate into the interior of the womb and either perforate the sac of the pregnancy or dislodge it from the wall of the uterus. Slippery elm bark is the common cervix dilator, and various domestic perforators—e.g., a knitting needle or a Higginson syringe—which will force fluid between the gestation sac and the wall of the uterus are the popular forms of intra-uterine instrument. Indeed an almost unlimited variety of instruments are in common use.

RISKS OF CRIMINAL ABORTION

All forms of criminal abortion are subject to dangers which may be grouped according to their time of development. Their frequency in 100 of my cases was as follows:

CAUSE OF DEATH IN 100 CRIMINAL ABORTIONS

"Immediate" death:	Vagal inhibition	11
	Air embolism	21
	Hæmorrhage	2
Delayed death:	Septicæmia (streptococcal 8, gas-forming 11)	19
	Pyæmia	3
	General peritonitis	27
	Confined local infection and toxæmia	12
	Tetanus	1
Indirect death:	Ictero-azotæmic syndrome	2
	Bacterial endocarditis	1
	Pneumonia and meningitis	1
	Total	100

Reflex shock, which comes on during instrumentation, is a vagal inhibitory reflex mechanism set in motion by receptors in the cervix or the body of the uterus stimulated by the contact of hot or cold fluid, by the touch of an instrument, or by sudden dilatation of the uterus by the injection of fluid. It is the more likely in an anxious fully conscious woman than in an anæsthetised one in whom the reflexes are abolished or diminished, and its sudden onset, with fatal arrest of heart-beat and respiration, catches the abortionist unawares, presenting him with the problem of a corpse. It is almost the only risk to which the really skilled professional abortionist is exposed.

Air embolism requires time for its development; for, after injection has placed the air under pressure between the pregnancy sac and the wall of the uterus, the air has to break into the exposed uterine veins, travel to the heart, pass through the lungs, and reach vital parts of the peripheral arterial and capillary circulation before collapse and death take place. Probably about 10 min. is required for this, provided a bulky volume is injected. During this time much of the oxygen of the air in circulation has become absorbed, the blood usually lacking the classical bright red colour, being dark plum-coloured. The occurrence of transient neurological symptoms from sublethal air embolism is recognised, but in criminal work only the fatal cases come to the notice of the pathologist and the quantity of gas is then considerable. Reports of such events (see Forbes 1944) have been confirmed by deaths after insufflation for medical purposes. The Higginson syringe is almost always the instrument responsible for air embolism, which is therefore common in both self-procured and the less skilled professional abortions. Air, sucked in as the fluid level in the basin or jug falls, is propelled under considerable pressure into the uterus when the nozzle lies in the cervix, and soap or lysol or other chemicals may enter the circulation with air and complicate the issue (Vance 1945). I have seen alum-fixation of the blood in such a case.

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Hæmorrhage is one of the uncommon causes of death and provides no novel pathological or medicolegal interest except for the situation and character of the rarer grave splits or tears following more violent interference. The usual forms of trauma, bruises, abrasions, shallow scratches, and blunt penetrations and perforations are not likely to cause much bleeding. They are most common in the least vascular parts of the canal, as the following figures from 100 successive cases of injury show:

Vagina	*Fornix*	*Cervix*	*Endo-uterine*	*Fundus*
15	4	48	12	21

The placental bed does not become developed until the third month, and is still comparatively small at the fourth month. The vast majority of criminal abortions are procured between the second and fourth months.

Infection is the commonest fatal complication, accounting for 64% of this series of 100 cases. When the filthy circumstances of many instrumental interferences are considered, this is no surprise.

In one fatal case I examined, a gum-elastic catheter had been passed by a habitual abortionist, aged 72, on a young girl, aged 26, in the dim light of a single compartment of a public-house lavatory without any preparation to combat infection. The catheter came unwrapped out of a handbag.

Trauma adds to the likelihood of infection, especially when the tissues are damaged by the additional injection of some corrosive fluid. The protective value of a germicide may be outweighed by the damage it does to the tissues. Indeed it is not uncommon to see burning by corrosive or scalding by hot fluid, or both combined, as a basis for infection.

The use of fingers to facilitate the introduction of an instrument (itself soiled) and the proximity of the anus are clearly potent causes of infection, and the bacteriology of septic abortion reflects this very clearly. Streptococci and *Clostridium welchii* or other gas-forming organisms, often in company with *Bact. coli communis*, account for the vast majority of infections. Butler (1943) emphasises the predominance, in severe infections, of *Cl. welchii*, 80 cases giving positive swabs from the vagina, and 23 out of 26 cases giving a positive blood-culture. Gas-forming infection develops with fulminating rapidity and is certain to reach the blood-stream within 24–36 hours, often less. Jaundice and hæmoglobinuria, with suppression of urine, are common in *Cl. welchii* septicæmias, and may divert attention from the real issue, but gas-forming septicæmia is commonly fatal without these signs.

The spread of less active pyogenic infections into the interior of the womb, its sinusoids, and broad-ligament veins, often assisted by spread to the pelvis by thrombophlebitis in the wall of the uterus or in the pelvic veins, is common knowledge. But it is not so commonly remembered that distant systemic infections—e.g., pleurisy and empyema, meningitis, septic phlebothrombosis and thrombo-angiitis migrans, bacterial endocarditis, septic pulmonary embolism, pyæmia, metastatic ophthalmitis, arthritis, indeed almost any infection—may have been set roving from a uterine infection following an abortion. It is for this reason that the statistics of septic abortion and the morbidity-rates of abortion as a whole are so unreliable. Deaths from bacterial endocarditis may be registered as such without their possible connexion with a recent abortion being suspected, and similarly the variety of "metastatic" infections detailed above. Berle (1942) says, "Deaths following abortion constitute nearly a half of all maternal deaths from septicæmia," and one is tempted to add "if the possibility is remembered."

One type of infection is of special interest. Tetanus may develop because of introduction of the organism in slippery elm or in wood-wool, or from the flora of the rectum. *Cl. tetani* is not rare in the human colon, and tetanus infection of injury by instrument to the womb is also not rare. Weinstein and Beacham (1941), reviewing 170 cases, found an average incubation of 6–12 days. Lapauze (1919) collected from French reports 19 cases of tetanus, of which 14 followed abortion.

Sterility.—Abortion may also cause sterility. Continued endometrial sepsis, polypoid endometritis, tubal block, and residual tubo-ovarian sclerosis are common consequences of trauma and infection. The large-scale experiment in induced abortion made possible in Russia by legislation in 1918 was terminated in 1935, partly on the grounds of ill health. Mulherin (1941) cited the view that since the legalisation of abortion there had been an increase in sterility, ectopic pregnancy, and "pelvic invalidism." The operation of dilatation and curettage under the best conditions is said to cause some 9% of women to become sterile.

CONCLUSION

The principal dangers of abortion will remain unchanged so long as it is unlawful to induce it for mere social or economic reasons, for it will be done secretly with limited skill, under conditions which encourage infection, and without the advantages of skilled care or modern protective chemotherapy.

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CONSCIOUSNESS AND ITS DISTURBANCES

CONSIDERED FROM THE NEUROLOGICAL ASPECT*

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(*Concluded from p. 6*)

Unconsciousness in Concussion

Let me refer for a moment to another topical matter. Denny-Brown and Russell (1941) focused attention on the disturbances caused by concussion in the vital reflex mechanisms of the brain stem, and in consequence there has been a tendency in recent work to discount the participation of the cerebral cortex in concussion and to attribute nearly all the immediate effects of a blow on the head to lower mechanisms. Now I think it cannot be too strongly emphasised that all parts of the brain and all the contents of the skull must share in the effects of the impact. I see no reason why the effects on cortical mechanisms should be less than on brain-stem mechanisms. Moreover, in consequence of the inevitable deformation of the skull in the average case at the moment of impact, the cerebrum has also to sustain the effect of an immediate intense compression, to which are added the effects of movements of fluid. Williams (1941) has shown that at the time of concussion in the animal, and in man as soon as electro-encephalography is practicable, there are profound changes in the electrical activity of the cerebral cortex, and, what I think is most important, these are of the same nature over the whole cortex as those occurring locally in a case of restricted cortical injury. In other words, the electrical records suggest a physical injury of the whole cortex. The

* The Lumleian lectures for 1947 delivered at the Royal College of Physicians of London on April 15 and 17, 1947 (slightly abbreviated).

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injury is fortunately in most instances reversible. We must in this connexion recall Greenfield's (1938) demonstration of wide areas of demyelination in the cortex after severe concussion. There is all this evidence that the cortex shares in the effects of the blow and, even if the brain stem and the hypothalamus are concussed, the cortex must surely be concussed too.

Sectional Disturbances of Consciousness

Disturbances of consciousness such as pathological sleep and coma are disturbances of the whole of consciousness. The conscious mind reacts to sleep as a whole, and such disturbances we call "global" disturbances of consciousness; but there are others which I will call "sectional disturbances." We may perhaps compare consciousness with the function of sight. It makes all the difference in the world whether a person has any vision or not, and he may have global disturbances of vision—disturbances of the acuity of vision—of all degrees. But he may also have disturbances of his visual field, and these are usually sectional. This is not to say that vision itself is sectional, but these particular disturbances are sectional, and if they become extensive enough they eventually abolish vision altogether. So it is with consciousness. The observations that I will refer to under this heading involve loss of awareness of a part of the self or of its environment. In calling them "sectional disturbances of consciousness" I do not suggest that consciousness is sectional. Undoubtedly it is not, for the whole consciousness may be kept active by sufficient remaining excitatory influences; but, if enough sections are lost, consciousness is lost altogether.

DISTURBANCES OF THE BODY IMAGE

Each of us has a mental image of his body, which was called by Head and Holmes (1911–12) "the body image." It is at the best of times only approximate and in some respects surprisingly vague. As regards our hands and faces and the fronts of our bodies it is fairly definite, but for parts which we seldom see, such as our backs, or to which we pay little attention, such as our feet, it is very indefinite. The image of the body in movement is far from precise; hence we have little idea of the exact position of our limbs even in walking. This image which we form for ourselves depends on impressions from the postural (proprioceptive) system and from the sight of our own bodies or their reflections. But it is greatly influenced too by our observations of other people whom we identify with ourselves. In certain conditions of disease this bodily image, never very accurate, may become grossly disturbed and depart grossly from reality. The disturbances are of four kinds: (1) a part of the body may be lost entirely from consciousness and so neglected altogether in the body image; (2) it may be only partially lost from consciousness; (3) a part of the body may seem normal in the body image when, in fact, it is paralysed (this may occur either because the patient has completely lost awareness of the part or because he has a "phantom" part—an active illusion of a normal part); and (4) a part of the body which is absent—e.g., an amputated limb—may still be present in a subject's image of his own body, thus constituting a phantom. In 1941, while acting as neurologist to an Army command of the Home Forces, I saw with Major J. D. Spillane at Aldershot two cases in which the patients were unaware, or partially unaware, of paralysed parts of their bodies, in each instance the left side. Since Major Spillane (1942) published an account of his cases, the record is available and I will make use of it.

The patient in the more severe case was an officer cadet who had a subarachnoid hæmorrhage which caused a temporary paralysis of the left side of his body, with partial sensory loss on the affected side, and some impairment of consciousness. One morning he told Major Spillane that there was no room for "him" (some other person) between his own body and the wall. It soon became evident that he thought this other person was "somebody in bed—over here" (pointing to his left side). Asked how long this "he" had been there he replied "All the time—he moves about." This delusion persisted all day. That evening he became violent, and, evidently unaware of his paralysis, tried to get out of bed, and fell on the floor unconscious.

Next morning he had left hemiplegia, and lumbar puncture showed a recurrence of subarachnoid bleeding. Little voluntary movement was possible in the left arm and leg but the left side of the face was not much affected. His head and eyes were turned to the right, and he talked volubly and was euphoric. There was general diminution of response to touch and pinprick over the left side of the body, but responses were variable, and stimuli, especially pinpricks, were often incorrectly interpreted. Position sense was much reduced in the left arm and was definitely poor in the leg. He often indicated with his right arm that he thought he had been touched on the right thigh, whereas he had been touched on the left thigh. The patient did not realise that he could not move his left arm and leg. When asked to move his right arm and leg he did so correctly, but when asked to move his left limbs he moved the right. Asked how his left arm and leg felt he replied "Fine." When told that he could not move his left arm and leg he smiled and said "That arm is all right." When his left arm was held up for him to see it he said "That was the one—he presses on me—these beds are small."

During the next few days his general condition remained unchanged. He persisted in asserting that his arms and legs were not weakened, and on several occasions he was forcibly restrained from getting out of bed. Five days after the onset of the hemiplegia, when there was slight return of power, he was persuaded after much argument that the paretic limbs held up for him to see were his own; but, when they were covered up again and he was requested to move them, he merely moved his right limbs. He eventually made a good recovery and left hospital eight months after the onset of his illness.

This case showed at different times several of the kinds of disturbance I have listed. During most of the period we are concerned with the patient gave no indication that he was aware of his left arm and leg except perhaps as parts of a supposed other person. He did not recognise them as his and he did not realise that he could not move them. When pricked on the left side he felt the prick but attributed it to that part of his body of which he was still conscious. He was unaware of the paralysis, probably because he was unaware of the affected limbs, but conceivably because he had "phantom" limbs.

The earliest cases of this kind which were described (Pick 1898, Babinski 1918) were cases in which the patient did not recognise the paralysis, and the condition was named by Babinski "anosognosia"—imperception of disease. Though we now recognise cases (and Babinski's may have been one of them) in which the limbs or a whole side of the body, and not merely the paralysis, have passed out of consciousness, we continue to use the same term to cover the different varieties of the condition.

In a milder form the disorder may be merely a periodic "forgetting" of a limb and can be corrected by persuasion and argument. In such cases the limb disappears from the attention rather than from consciousness. A minimal degree of this disturbance is the state in which the patient, though aware of a stimulus applied to an affected limb under conditions of attention, does not recognise a stimulus applied to it if his attention is diverted, as by application of a similar stimulus to the other side of the body at the same time. He is not nearly so conscious of the affected limbs as of those of the sound side.

In all the recorded cases of imperception of hemiplegia the paralysis was on the left side. Necropsy reports are available for only four such cases, and in every one of these there was a lesion of the right thalamus (Pick 1898, Pötzl 1924, von Hagen and Ives 1937).

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It will be remembered that a lesion interrupting the thalamocortical connexions abolished the electrical activity of the area of cortex concerned, and in all of these cases the portion of cortex on which the affected part of the thalamus projected was the posterior part or the whole of the parietal lobe. The area concerned with total or severe loss of consciousness of half of the body seems to be an area in the parietal lobe farther back than the postcentral gyrus—in the parieto-occipital association area. Each part of the opposite half of the body is evidently re-represented for certain purposes in an area in and above the supramarginal gyrus. In some cases in which the disturbance was less extensive the lesions have been in the posterior parietal cortex.

In the case I have described and in others of this kind, when a stimulus is applied to the affected side, something is experienced by the patient but it is not related to the left side and it does not occur to the patient either that he has a left side or that he has no left side. This degree of disturbance has rarely, if ever, been recognised on the right side and, as Holmes (1946) has suggested, it may not be detected when accompanied by aphasia.

There are many matters about such cases which call for discussion, but I am concerned at present with only one aspect, and I have recounted this case for the sole purpose of asking one question: what would happen if the patient lost the awareness of both halves of his body? He would then be to himself a disembodied spirit. Can you imagine yourself without any body-consciousness? To yourself you could be a disembodied spirit, entirely devoid of body. I find that I am quite unable to imagine myself as such. I can imagine myself possessed of a body of which I was unaware by bodily sensation, and then I would, I suppose, if I remained conscious at all, still be aware of my environment—through eyes and ears of which I was unaware—and I might see my body as I see that of another person. But could I remain conscious if I had no awareness of my body as me? Certainly a large part of consciousness would be lost. We can put aside the idea that I would remain conscious of my thoughts, for it is generally agreed that we cannot detect any awareness of mental processes; all awareness of self seems to be bodily. Would the visual and auditory stimuli from the environment be sufficient to keep me awake? The patient referred to in my first lecture who had a hæmorrhage in her pons and must have been completely deprived of the feeling of her body was unable to maintain consciousness and died—it is true she had lost her hearing as well—and the same occurred in Bremer's animals. It is generally agreed that consciousness is so dependent on bodily sensation that it could not be maintained in its absence.

One other point is worth noticing. In cases of anosognosia (and in the double case I have imagined) the loss of sensation may not be complete, but it is essentially and predominantly a proprioceptive loss, so that proprioceptive sensation is apparently of dominant importance for consciousness of our bodies.

DISTURBANCE OF AWARENESS OF THE ENVIRONMENT BY VISION

The person who has lost vision has lost a very important means of awareness of the environment; but what the blind person loses above all is the power of seeing objects in the environment. The essence of the environment, however, is not objects but space; and since the bodily self occupies part of space, the environment is even physically inseparable from the self. What is so remarkable is that it is possible for a subject who is not blind to lose the power of seeing objects in spatial relationship to each other. Such cases have been reported by Holmes and Horrax (1919) and by others. The following is the most complete example that has come under my notice:

In 1937 I saw a woman of 40 at the National Hospital and subsequently she was admitted there under my care. She had been quite healthy until 2½ years before that, when in the 8th month of pregnancy she had two fits during the night. She remained unconscious and was admitted to hospital, where she gave birth to a dead child that day. For three or four weeks she lay as if asleep and appeared hemiplegic down the left side. She had complete amnesia for three weeks after the fits. When she came round she could not lift her left arm off the bed and could not use her left hand. Her left leg was weak, but she could move it up and down in the bed. She also had a disturbance of her sight and of her movements.

She had no difficulty in recognising objects or in appreciating their significance, but she could not appreciate the nearness or distance of an object or its position relative to other objects. At first, being unable to locate objects she saw, she could not pick up an orange off the table though she could see it. She had particular difficulty with the lavatory chain; she knew it was there, but she would keep losing sight of it and grope all over the place for it. She bumped into things and could not get past them, and she had difficulty in going through a door or finding the door in a room, except by groping round the wall. When led about she did not know how far a motor-car was away from her, and had no idea of her position in relation to it or the road.

She was willing and coöperative and a good witness, and had good insight into her disability. She had no obvious emotional change. Her memory was good, and her speech was normal. She had some weakness of the left side of her face and of the left arm, the latter affecting the proximal muscles. Appreciation of light touch, pinprick, and posture of her extremities, tactile localisation, stereognosis, and vibration were all normal. Her tendon-jerks were greater on the left side, and the left plantar reflex was indefinite, the right being flexor.

Ordinarily she had to be led about but if she was started off where there were no obstructions she could walk unaided—e.g., across the ward—and then walked normally. She could not read, being unable to locate a word or consecutive words, but a single word (of a newspaper heading) presented separately might be recognised. She could not locate the vision testing-card when it was held up in front of her. She sometimes understood a picture or an object in a picture. She was unable to count objects by looking at them, but counted them normally if she felt them. She could not write and could not copy a simple design such as a circle or a cross, and could not join two points on a paper with a pencil or divide a line or even put the pencil on a line (this applied to both hands equally). She could read the clock, but she said that she saw the time at once or failed to do so; the more she looked at it the more muddled she became. She had homonymous defects in her left visual fields, absolute on the left lower quadrants and relative in the left upper quadrants. Her optic fundi were normal. She had great difficulty in putting on her clothes and she thought this was because she could not tell which way up a garment was.

In another patient the same disturbance of sight came on towards the end of pregnancy, the onset being associated not with convulsions but with a period of stupor. This patient eventually made a partial recovery and, though the disturbance was still present on one half of her visual field, the other half having become normal she was unaware of any disability.

Brain (1941) has described cases in which the patients, having lost the power of localisation in the left half of the visual field, and having some impairment of postural sensibility on the left half of the body, were apparently unaware of the left half of external space. Each of these patients got lost on going from one room to another in his own home, always making the same error of choosing a right turning instead of a left, or a door on the right instead of one on the left. His attitude to the left half of the external space was one of inattention or neglect; in walking he behaved as if it were not there, but in conversation he recognised its existence. It appears from these cases that a severe disturbance of awareness of the left half of space may so disrupt spatial perception that the patient does not recognise his surroundings.

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Like my first patient, Brain's patients had a particular difficulty in dressing themselves. In all these instances the patient, because of the difficulty in spatial appreciation, could not adapt the garment to his body scheme.

The appreciation of space by vision is probably an educated function depending on the coördination of visual impressions with those derived from postural sensibility. The lesions which abolish it are believed to be situated in a small portion of the parieto-occipital association area on each side. Both of my patients must have had bilateral lesions (probably due to venous thrombosis), but the second one recovered sufficiently on one side to regain spatial appreciation in the corresponding half-fields.

What would have been their state if postural sense too had been lost? Each of them would then have been unable to appreciate space, even the space occupied by her own body—a condition which it is very difficult to imagine and which, from what we have seen earlier, is probably inconsistent with the maintenance of consciousness. If we suppose for a moment that the patient could remain conscious, she would, like our previous imaginary patient, feel as a disembodied spirit, but in this instance, though she might see her body as an object, having lost the appreciation of spatial relationship she would be unable to relate it to "herself" (whatever "self" remained to her). Such cases emphasise the importance for consciousness of the parieto-occipital association area and, in a new way, the importance of the postural (proprioceptive) sensory system.

Disturbances of consciousness referable to other sensory systems might be cited.

In 1931 I had a patient who, it seemed in consequence of a cerebral hæmorrhage, became for a time word-deaf. He had a lesion on the left side which must have caused a functional interruption of his auditory radiation, and it caused also a sensory impairment on the right half of his body and a partial loss of the right halt of his visual field. During his illness he talked almost continuously in a jargon of half-formed words, and he told me afterwards that he had been unaware that he was talking.

Here we have unconsciousness of an activity—viz., unconsciousness of speech—depending on word-deafness and probably also a postural sensory loss resulting from a lesion in the dominant hemisphere.

Limitations of Normal Consciousness of the Body

It is well known that the positions of the parts of our body at any moment are revealed to us by our postural sense, which has its anatomical substratum in the post-central gyrus. The limitations of our consciousness in regard to movement are revealed in cases in which postural sensation is abolished on one side of the body.

Bartlett (1947) drew attention to the fact that the performer of a skilled action had in general no idea how he performed it. The matter goes much deeper than that, because we have no idea how we perform the simplest action. If I wish to bring my forefinger to the point of my nose, I have no idea by what means the movement is executed; I will it, and it is performed. What muscles are employed, what reserves of power each has to call upon, how they are coördinated—of all that I perceive nothing whatever. I may at any moment by my postural sense appreciate the position of my hand in the course of the movement, but that is all. It is as though the commander of an army ordered a certain movement to be executed and thereafter had no knowledge of the activities of his executives, except in so far as the points they had reached were reported to him by his intelligence service. The executives have their own means of information, which are, however, unknown to him, because even a simple muscle twitch changes in character if the afferent fibres from the muscle are divided. When the postural sense in a limb or in one side is abolished, some interesting effects are observed. William James recorded that, if a patient who had lost sensation in one arm was asked to put the affected hand on top of his head while his eyes were closed, and was at the time prevented from doing so, he was very surprised on opening his eyes to find that the movement had not been performed. I have made several observations of the same kind.

A patient whom I have at hospital at present is devoid of postural sensation in her right lower limb. If, when she cannot see the limb she is asked to raise it from the bed, and at the same time movement is prevented, she feels that the movement has been carried out, and will state that the foot is being held 6 in. above the bed.

It is thus as if a movement ordered by the commander was recorded in consciousness though he had no information that it had been carried out. It is easy to see that this may be developed as a conditioned reaction, because the commander is so accustomed to his commands being executed. It is evident that this is a variety of phantom phenomenon, and Riddoch (1941) has referred to similar instances but it is not quite the same as the true phantom phenomenon which depends on false afferent impressions.

I emphasise that all the executive activity of movement is outside consciousness. Of the simplicity or complexity of the components we have no idea. In the absence of postural sensation we know nothing of it at all, and even with full possession of sensation the information that is brought into consciousness is very limited, and all that we get to know is the resultant of all the component activities.

On the sensory side also all that we become conscious of in regard to our bodies is the resultant of an infinite number of component sensations which remain below consciousness. Let me quote Sherrington on this point:

"The main sensual basis of the awareness of the limb and its posture rests, as disease and experiments show, on the sensory nerves to the motor structures in the limb. Of such nerve-fibres there are many thousands, and they individually register the tension at thousands of points they sample in the muscles, tendons, and ligaments of the limb. These keep on firing into the nerve centres impulses reporting, so to say, the tension of thousands of sample-points within the limb. In my awareness of the limb and its posture, and similarly in my awareness of its movement when it moves, I perceive no trace of all this. In 'experiencing' the limb, I find no hint of this multiplex origin of the percept, no additive character in it, no tale of tonsions within the limb, or of its possessing muscles and tendons. I am simply aware of where the limb is, and when it moves—or is moved . . . the percept is not a very vivid one."

Conclusions

I indicated at the beginning that my intention was not to philosophise but to present observations. Possibly some or all of the observations may be capable of interpretations other than those I have given them, but at any rate we seem to have a body of material which is consistent within itself, and the newer observations illustrating what I have called sectional disturbances of consciousness, fit into and amplify the theory to which it gives rise. Any adequate theory must be able to embrace new observations and even, in time, to predict new facts. The conclusion is that from the point of view of organic neurology consciousness depends on a process in which the cortex is kept in a state of activity by sensory impulses, and by an activation depending on the hypothalamus. It is a theory that has been used before in application to sleep.

Let us consider the elements in this theory briefly in the reverse order. The function ascribed to the hypothalamus is to keep the brain in a state of metabolism in which it is capable of being instigated to activity by

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the afferent impulses which reach it. In our domestic wireless sets and in all electrical recording instruments an electric current is necessary to render the instrument "live" before it is capable of receiving or recording any other activity; the hypothalamus we suppose controls such a power. This is a vegetative function, consistent with what we know of the other functions of the hypothalamus. The electro-encephalographists speak of the "driving" influence of the hypothalamus and find that when the hypothalamus is interfered with the cortical activity in which they are interested is universally abolished.

The next element is the afferent impulses. My observations indicate that without sensory excitations consciousness lapses—deprived of input the instrument is silent. They suggest that afferent impulses from the body are of overwhelming importance; although we can conceive that consciousness might be kept alive by visual or auditory or olfactory impulses from the environment, both clinical and experimental observations indicate that, in practice, without any awareness of the body consciousness is not maintained. If afferent impulses from a large portion of the body are interrupted or if conditions are such that the space which it occupies is not recognised, that portion of the body may pass out of consciousness and general consciousness be considerably impaired. While excitations from the environment are undoubtedly of great importance and may dominate consciousness, a proportion of impulses from the body would seem to be essential.

Thirdly, I think we cannot avoid the conclusion that consciousness is essentially associated with activity of the cortex. From time to time it has been suggested that the essential activity may be in the thalamus or the other basal ganglia or the grey matter around the third ventricle, but in every way in which we can test it disturbance of consciousness is associated with disturbance of cortical activity. That applies to partial as well as to complete losses of consciousness, and it applies to both the varieties of disturbances of consciousness (the negative and the positive) that we know. It corresponds with the electro-encephalographic findings, and these show us also that a disturbance in the thalamus would in any case involve a disturbance in the function of the cortex.

I think it probable that full consciousness involves a generalised activity of the cortex. Our observations have suggested that the parieto-occipital association areas are of quite exceptional importance for consciousness, but we have had evidence also that the frontal lobes are important for the awareness of self, and the other lobes, with their primary receptive areas, are of obvious importance for awareness of the environment, if not of the self. The idea that consciousness is not some "thing" within the brain, but depends on an activity—on a process going on—was developed considerably by Hughlings Jackson. I may quote two sentences: "Consciousness is not an unvarying independent entity; consciousness arises during activity of some of those of our highest nervous arrangements by which correspondence of the organism with its environment is being effected." And again: "There is no such entity as consciousness—in health we are from moment to moment differently conscious. Consciousness varies in kind and degree according as the parts of the brain in activity are different and according to the degree of their activity." The introductory phraseology reminds me of William James's expression years later: "Subjective consciousness is the name of a non-entity."

Observe that I do not say that consciousness *is* an activity of the cortex, for the cortex is material and its activities are material. It is associated with an activity of the cortex—it is a condition in which the cortex is active—but of the nature of the association between mind and brain we still have no idea. We have come, however, into very close agreement with the psychologists, for surely this condition of cortical activity is a counterpart of William James's "thought goes on." With those who insist on the subjective and objective aspects of consciousness, how do we stand? In regard to the former there is no difficulty. This activity of the cortex with which consciousness is associated is inevitably dependent on sensory excitations, and these sensory excitations bring an awareness of self and of the environment. But as regards subjective consciousness, our observations provide no evidence of any substance in the brain which is consciousness, or of any local structure—no evidence of anything that could be called an anatomical or nervous entity.

But what then is subjective consciousness. Who is aware? Who or what is "I, the knower"? The question is centuries old and you will not expect me to provide the answer, but towards what kind of ideas does the present knowledge of neurology direct our minds? Out of our proprioceptive and visual impressions we build up an image of our own bodies—imperfect, it is true, and apt to be disturbed by disease—an image built up by the summation of impressions from and about our bodies on which we come to rely. It seemed from our examples that we relied on it to such an extent that we could not maintain consciousness without it. Neurology in recent years has made much use of this concept—the body-image. Some body-image is evidently necessary for consciousness. In Sherrington's phase, the "I" is aware of itself as an *embodied* "I." The body-image, though inseparable from it, cannot be subjective consciousness; but is it not possible that "I, the knower" is a similar figment of our sensory impressions—a feeling, an image based on sensations and memories of sensations not from the body only, but from all our experience—something similar to, but more comprehensive than the body image, a "mind and body" image, a "self," but an image nevertheless?

This is not quite the same as the position taken up by William James when he wrote: "It seems as if consciousness as an inner activity were a postulate rather than a sensibly given fact, the postulate namely of a knower as correlative to all this known." The image must have as a substrate a pattern of activity, a pattern of facilitations throughout the brain—lines of action in the cerebral field. I feel that it has a little more substance than a mere postulate. On this image—if image it be—on this patterning of certain cerebral activity which we develop in our early years we become so dependent that without it we cannot survive as sentient beings.

In our generation even the physicists and mathematical philosophers have taken up the discussion of consciousness. Thus Eddington (1928), having resolved the whole of the material world into waves in the ether and vibrations in the atom, turned to consciousness in search of reality. "There is no question," he wrote, "about consciousness being real or not; consciousness is self-knowing and the epithet 'real' adds nothing to that."

This image that we build for ourselves, this "non-entity," this shimmer that floats over the active cortex with its waves of potential changes, is it any more real than waves in the ether or vibrations in the atom? Surely Eddington's successors must look elsewhere for reality.

Summary

There are two varieties of unconsciousness (and disturbances of consciousness). One (coma) is related to sleep and depressed cortical activity, and the other to convulsive phenomena and irregular cortical discharges.

Consciousness depends on activity of the cerebral cortex. I know of no evidence of consciousness in man from activity of other structures in the absence of

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cortical activity. Impairment of the activity of the cortex over a wide area leads to unconsciousness.

The activity of the cortex with which consciousness is assocated is maintained in some vegetative way by activity of the hypothalamus. Unconsciousness may therefore be caused by lesions of the hypothalamus.

The activity of the cortex with which consciousness is associated is maintained by afferent impulses in the sensory systems. Unconsciousness may be caused by interruption of the somatic sensory tracts in the upper half of the brain stem; this is probably because all awareness of the body is thereby abolished and some awareness of the body is necessary for consciousness.

Consciousness is usually associated with the presence of fast rhythms in the electro-encephalogram, and sleep and coma with the absence of such rhythms, but fast rhythms may be present during unconsciousness. Consciousness cannot be explained in terms of electronics, since the latter arise from the activity of matter, whereas consciousness is immaterial.

Unconsciousness in a fit or in a petit mal attack is associated with a widespread disturbance of cortical activity, with exaggerated electrical alterations. Unconsciousness after a fit is associated with extinction of electrical and other activity of the cortex.

The global disturbance of consciousness in concussion may depend on several factors, from among which a direct effect of injury on the cortex can certainly not be excluded.

Sectional disturbances of consciousness are due to the loss or the impairment of some afferent activity which abolishes the awareness of part of the bodily self or its environment. With each sectional disturbance of consciousness there is an associated localised disturbance of cortical activity. The postural (proprioceptive) sensory systems are of special importance for the maintenance of consciousness.

Dreamy states and psychical seizures are sectional disturbances and may be likened to double partial consciousness (one true and one false).

Much of our activity, especially all the execution of movement, is outside consciousness, but some record of movement willed may be made in consciousness, even if the movement is not carried out.

The change in personality resulting from prefrontal leucotomy may be due wholly or in part to a change in consciousness related particularly to affect and to the quality of "depth." The patient after this operation is less aware of his feelings.

Consciousness is associated as an epiphenomenon with an activity of the cerebral cortex which is maintained by sensory excitations. These excitations and the activity they rouse lead to an awareness of the bodily self and of the environment (objective consciousness). Subjective consciousness (I, the knower) is possibly a "body and mind" image analogous to the body image.

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TORULOSIS OF THE CENTRAL NERVOUS SYSTEM

REPORT OF TWO CASES

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THE improved outlook in the treatment of tuberculous meningitis with streptomycin (Medical Research Council 1948, Smith et al. 1948) has focused attention on the early diagnosis of chronic infections of the central nervous system. One such infection is due to *Torula histolytica* (*Cryptococcus hominis* or *neoformans*). Little known or seldom recognised in this country, human infection by these yeast-like organisms has often been reported elsewhere, over 120 cases of torulosis having been published. Two additional cases are described here in the hope that torulosis may be diagnosed more often if it is kept in mind. So far only 4 cases have been reported in Great Britain (Smith and Crawford 1930, Greenfield et al. 1938, Blair 1943, Magarey and Denton 1948), but there is little doubt that the condition is not so uncommon as this paucity of reports suggests.

Torulosis of the central nervous system was first described in Germany, by Busse and Buschke in 1895, but the greatest incidence has been in America and Australia. In Australia Cox and Tolhurst (1946) collected and described 13 cases in ten years. A diffuse chronic meningo-encephalitis is the commonest manifestation of the infection. Less common is the circumscribed granulomatous mass in the brain. Cox and Tolhurst (1946) reported 4 cases of this type. Only 4 cases had been described previously: 3 in the United States (Longmire and Goodwin 1939, Swanson and Smith 1944), and 1 in South America (Dickmann et al. 1942). To this number of discrete "torulomata" Krainer et al. (1946) added 1 in India, and Hassin (1947) 1 in the United States. Here we record the eleventh.

Torula organisms are spherical yeast-like fungi reproducing by budding. They are widespread—e.g., in milk and other foodstuffs—and Dr. J. T. Duncan (personal communication) has found them in the mouth and on the skin of healthy people. The conditions under which they become pathogenic for man and animals are not known. The disease may involve any tissue, but affections of the central nervous system account for half of the 60 cases reviewed by Levin (1937). Levin (1937) believes the lungs to be involved in 25% of cases, Cox and Tolhurst (1946) in nearly 60%. The infection is thought to gain entry through the respiratory tract in most patients and to lodge primarily in the paranasal sinuses or in the lungs.

CASE-RECORDS

Our first case may be regarded as typical of the diffuse meningo-encephalitic form of torulosis.

Case 1.—An electrician, aged 54, had had a scalp wound in 1939 which took several months to heal. In December, 1942,

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severe incapacitating headaches set in, with vomiting, irritability, fluctuating drowsiness, and dysarthria. The pulse-rate was slow (50–60 per min.) and temperature raised (100–101°F), and the patient lost weight. There was no neck rigidity.

In February, 1943, the patient had epileptic attacks, possibly of focal character. On admission to the Nuffield

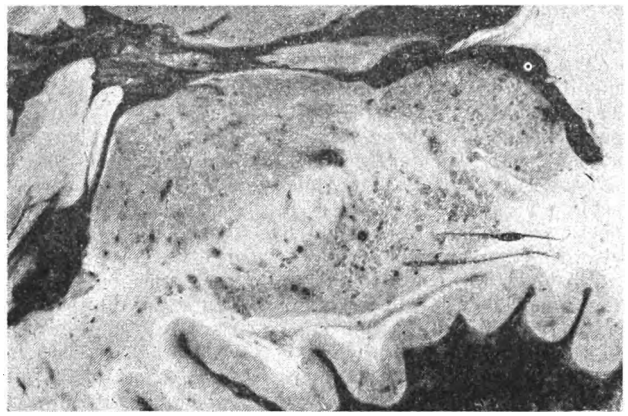

Fig. 1—Basal ganglia in diffuse meningo-encephalitic type of torulosis showing honeycomb appearance due to gelatinous masses (case 1).

Department of Surgery on March 1, 1943, he was emaciated, comatose, and moribund, with Cheyne-Stokes respiration, a steadily rising temperature, a feeble and rapid pulse (130–150 per min.), and a blood-pressure of 100/85 mm. Hg. There was still no neck rigidity. The patient had bilateral papilloedema of 4 D, a slight right facial weakness, flaccid limbs, absent tendon-jerks, and flexor plantar responses. Lumbar puncture was not performed because of the papilloedema, but a ventricular tap produced cerebrospinal fluid (C.S.F.) under a pressure of 600 mm. H_2O, slightly turbid, with protein 35 mg. per 100 ml.; 264 cells per c.mm., mainly lymphocytes; chlorides 690 mg. per 100 ml.; sugar normal; Lange curve 01222110; Wassermann reaction positive; and torula organisms in large numbers, which grew well on culture. The patient died fourteen hours after admission.

Necropsy showed abundant torulæ in the exudate found in the ethmoidal air-cells. There was no evidence of torula infection, and no relevant abnormalities, in any organs other than the brain. The brain was slimy to touch, and ill-defined grey gelatinous areas up to 1 cm. in diameter were present in the sulci. The meninges showed a milky opacity, which was less definite over the base than over the convexity. There was a gelatinous cyst 0·2 cm. in diameter over the left temporal pole. Pin-point and pin-head grey gelatinous masses were scattered throughout the basal ganglia (fig. 1). In the subcortical white matter the perivascular sheaths were distended by gelatinous grey material. A few pin-head granulomata were visible in the ependyma. The ventricles were not dilated; the brain as a whole was slightly congested, the main cerebral vessels being normal. Collections of gelatinous material were also present in the dentate nuclei of the cerebellum. There was gelatinous thickening of the arachnoid and focal congestion of the white matter of the spinal cord.

Circumscribed "toruloma" of the central nervous system, the less common type of lesion, is illustrated by our second case.

Case 2.—A miner and lorry driver, aged 50, had been treated for pulmonary tuberculosis at the age of 20. In 1943, two years before admission, he had had a productive cough, with hæmoptyses and occasional recurrent pleurisy. Eight months before admission a wedge-shaped interlobar opacity in the left lung had been found radiographically. Two months' later, in August, 1944, he had developed headache, neck stiffness, fatigue, dizziness, slurring of speech, and unsteadiness of gait, and had had to stop work. By December, 1944, he had deteriorated, and now he complained of vomiting and diplopia besides his previous symptoms.

On admission to the Nuffield Department of Surgery on Feb. 1, 1945, he was prostrate, wasted, pale, and mildly confused. Temperature 97°F, pulse-rate 100, respirations 20 per min. There was no definite neck rigidity or Kernig's sign. The nasal margins of the optic discs were blurred, and there was diplopia on looking to the left, with difficulty in maintaining lateral conjugate movements of the eyes, and gross restriction of upward movement; nystagmus was present on lateral deviation, slow and coarse on looking to the right. The pupils were normal. There was gross slurring dysarthria and also gross ataxy and hypotonia of the limbs, more pronounced on the left. The patient could not sit up unaided. The tendon, abdominal, and plantar reflexes were normal. He had a slight non-productive cough, with diminished air entry and dullness over the mid-zone and base of the left lung. Radiography of the chest showed an area of consolidation in the mid-zone of the left lung (fig. 2). Radiography of the skull revealed an opacity of the frontal sinuses, thinning of the dorsum sellæ, and large venous emissary channels at the torcular. Lumbar puncture produced C.S.F. under a pressure of 180 mm. H_2O, with 95 cells per c.mm. (lymphocytes 88); protein 160 mg. per 100 ml.; chlorides 700 mg. per 100 ml.; sugar diminished; tryptophane reaction strongly positive. No organisms were found.

The differential diagnosis lay between abscess, tuberculoma, or neoplasm of the left cerebellar lobe.

Operation.—On Feb. 9, 1945, a cerebellar exploration was performed. Both cerebellar tonsils were found to be broadened and herniated through the foramen magnum. The left cerebellar lobe was larger and firmer than the right. The cerebellar folia on both sides showed yellow discoloration, and the arachnoid was irregularly thickened. A brain needle inserted into the upper part of the left cerebellar lobe encountered resistance at a depth of 2 cm. from the surface. After the needle was advanced another centimetre or two, yellowish-white rather tough and gelatinous mucopurulent material was aspirated. The mass was easily exposed by removing the overlying cerebellar tissue (fig. 3). It had a smooth greyish-brown surface, and coursing over it were a few blood-vessels. Small fragments were removed from the surface of the mass for biopsy. There was no bleeding. The fragments were slimy and gelatinous but tough and difficult to spread between the two glass slides used for the wet-film technique. The films (fig. 4) showed great numbers of closely packed encapsulated torulæ. In the narrow interstices between the torulæ were cells with small nuclei; occasional foam-cells and multinucleated giant-cells were also seen. The granulomatous mass was next enucleated. The upper pole was lying under the

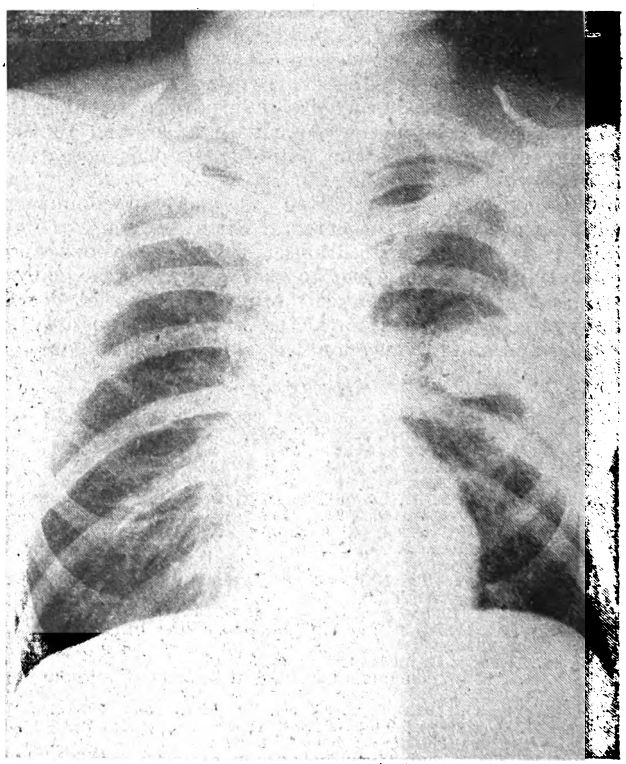

Fig. 2—Radiogram (March 14, 1945) of chest showing opacity in left mid-zone (case 2).

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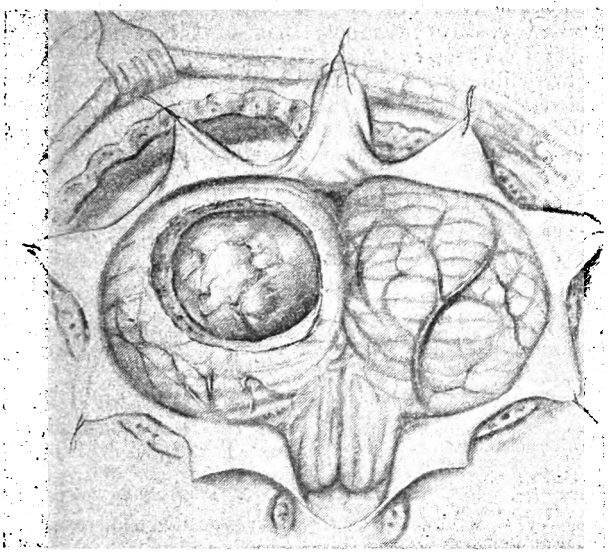

Fig. 3—Circumscribed toruloma exposed at operation on Feb. 2, 1945 (case 2).

tentorium and covered by arachnoid only. The deep surface was coarsely nodular like some meningiomas, yet had hardly any vascular connexions with the cerebellum. Owing to its friability some of the mass had to be removed piecemeal, but the greater part came out in toto. It was firm and slimy, while fresh.

Pathological Examination.—After fixation the size of the bun-shaped mass was 4·5×3·5×3·5 cm. The base was covered by flattened cerebellar folia showing some subarachnoid hæmorrhage, and the nodules on its deep aspect were glistening and semitranslucent. On section a peripheral zone of clear grey semitranslucent, tough fibrous tissue was seen. Deep to this was soft grey gelatinous material flecked with white irregular areas of pin-head and larger size. The outline of the soft central part was scalloped. In the centre of the mass was a hæmorrhagic cavity.

Microscopically, the central parts of the mass showed great numbers of rounded encapsulated cells each containing several small highly refractile bodies. Round the cell body was a narrow band of refractile material, and outside this a wide unstained zone (the capsule), usually greater in width than the diameter of the cell. Occasional budding of the cells was seen. Clumps of these typical torulæ were separated from each other by fine irregular bands of collagenous tissue, and the whole mass was divided into loculi by denser and broader bands. Round the loculi was a zone of granulation tissue composed of chronic inflammatory cells, plasma cells predominating; there were also fat-granule cells, eosinophils, some cells of epithelioid type, and occasional multinucleated cells. There were some small foci of necrosis. The capsule round the whole mass was thin and composed of collagenous material infiltrated by chronic inflammatory cells.

The adjacent cerebellum showed great loss of Purkinje cells, with some œdema and gliosis. There was moderate infiltration of the leptomeninges by chronic inflammatory cells.

Progress.—A fortnight after the operation the patient could walk unaided, his confusion, dysarthria, diplopia, and nystagmus having subsided. The C.S.F. now showed 160 cells per c.mm. (lymphocytes 76%); protein 180 mg. per 100 ml.; sugar diminished; chlorides 670 mg. per 100 ml. No torulæ or other organisms were found in the C.S.F., but a nasal swab showed abundant torulæ. Four weeks after the operation the patient was discharged to a convalescent hospital, from which he was removed later by his relations. In the convalescent hospital he developed occasional rises in temperature from 101 to 102°F, and four months after operation he had relapsed into his preoperative condition.

On readmission to hospital on June 1, 1945, his neurological condition was similar to that on his first admission. In addition the patient had enlarged lymph-nodes in the right axilla and a mass in the left iliac fossa. The cerebellar decompression was slack. Radiography of the chest showed progression of the pulmonary lesion. The C.S.F., on June 2, contained 5 cells per c.mm.; protein 1000 mg. per 100 ml.; chlorides 580 mg. per 100 ml.; and no sugar. On July 3, the C.S.F. showed 82 cells per c.mm.; protein 1000 mg. per 100 ml.; chlorides 560 mg. per 100 ml.; and was under a pressure of 80 mm. H_2O. Again no torulæ were isolated from the C.S.F., but they were found in large numbers in the nasal and pharyngeal secretions.

On July 9, 1945, the patient was transferred to Mount Vernon Hospital, Northwood, for deep X-ray therapy of the chest. He died three weeks later, five and a half months after operation, and about a year after the onset of intracranial symptoms. Permission for necropsy was refused.

DISCUSSION

Diagnosis.—It is evident from these and previously reported cases that the presenting clinical picture is confusingly similar to that seen in tuberculosis of the central nervous system. Severe headaches, occasional epileptiform manifestations, mild papilloedema, cranial nerve disorders such as oculomotor palsies and dysarthria, and pyramidal and cerebellar signs are in their diversity and variability similar features of both affections.

The long-standing symptoms and signs of lung infection in case 2 strongly suggested tuberculosis. Cox and Tolhurst (1946) mention 2 cases as having had lung symptoms for over twelve years. Moreover, in 1 of their cases of verified torulosis Koch's bacillus was found in the sputum; hence the diagnosis was further confused by the coexistence of the two similar diseases.

Examination of the C.S.F. may show the lymphocytosis, the tendency to high protein and low chloride levels, and the meningitic Lange curve, which are often though not always found in tuberculous meningitis (Smith and Daniel 1947).

A further diagnostic difficulty arises in the microscopical examination of the C.S.F. Torulæ may not be present—e.g., our case 2, 2 cases of Cox and Tolhurst (1946), and Hassin's (1947) 2 cases—or the torulæ, though seen in films, may be misinterpreted as lymphocytes. This may the more easily happen if the possibility of infection by torulæ is not borne in mind. Finally, according to Cox and Tolhurst (1946), it may be impossible to prove the presence of some strains of this

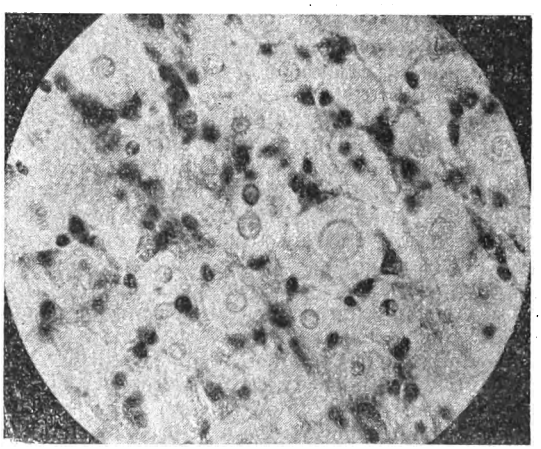

Fig. 4—Photomicrograph of wet-film preparation made at time of operation showing torulæ surrounded by wide clear capsules and containing refractile bodies (case 2). Note torula dividing by budding in centre of field.

organism, except by very protracted culture. Material from both our cases grew readily on culture.

A curious finding in case 1 was the positive Wassermann reaction, but too much weight cannot be placed on this since it was only a single observation. Not more than about 10% of the published cases had Wassermann reactions tested, and these were all negative except 2 cases reported by Cox and Tolhurst (1946).

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EFFECTS OF VARIOUS AGENTS ON CULTURES OF TORULA

Culture	Crystal violet 1:3,125,000	Soluthiazole 20%	Soluthiazole 4%	Propamidine 1:12,500	Penicillin 1000 units per ml.	Streptomycin 1000 units per ml.
C.neoformans (case 1, brain)	+	+	0	+	0	0
C.neoformans (case 2, brain)	+	+	+	+	0	0
C. neoformans (case 2, nose)..	+	+	+	+	0	0
C. neoformans (strain X)*..	+	+	0	+	0	0
C. neoformans San Felice*..	+	+	0	+	0	0
C. hominis Vuillemin* ..	+	+	0	+	0	0

+ = Inhibition. 0 = No inhibition.
* Supplied by Dr. Duncan.

An intracranial space-occupying lesion is often suspected in torulosis owing to signs of increased intracranial pressure. The finding of one or more tumour-like masses, both in the hemispheres and in the cerebellum, has been reported in 10 cases. Such a tumour has been extirpated in only 2 cases previously (Swanson and Smith 1944, Krainer et al. 1946).

It is surprising that in case 2, in which the torular mass was opened at operation, torulæ were not disseminated throughout the cerebrospinal pathways (torulæ were never subsequently found in the C.S.F.). Here again a curious parallel is seen with tuberculosis, since tuberculous meningitis does not of necessity follow even incomplete removal of cerebral tuberculomata (Smith and Daniel 1947).

Treatment.—Freeman (1931) has pointed out that torula is one of the most resistant parasites of man. Its biological characteristics are such that none of the usual physical or chemical agents will affect it either in vivo or in vitro; and it does not call forth effective antibody or cellular reaction. Jones and Klinck (1945) stated that neither sulphadiazine nor penicillin had any inhibiting effect on torulæ in vitro, and that gentian violet was ineffective in their case.

The effects of various agents on cultures of torula from the present cases and on strains provided by Dr. J. T. Duncan are shown in the accompanying table. Sulphadiazine, sulphapyridine, sulphathiazole, 'Sulphamezathine,' sulphanilamide, and sulphacetamide were also tested, and did not produce any inhibition in concentrations up to 10 mg. per 100 ml. From the table it may be inferred that mould products such as penicillin and streptomycin are unlikely to have an effect on these fungi. Of the sulphonamides used in these experiments only 'Soluthiazole' was effective in vitro. Crystal violet (gentian violet) inhibited all strains in a dilution of over 1 in 3,000,000. This suggests that in-vivo trials with gentian violet might be undertaken. It will be recalled, however, that in the body torula organisms have thick capsules, which disappear on culture. The organism is therefore probably more vulnerable in vitro, and conclusions from experiments in the laboratory may not be borne out by results of treatment.

Surgical excision is justified and may be successful in cases with isolated toruloma, as it appeared to be in the case reported by Krainer et al. (1946). In our case 2 removal was temporarily successful, and the patient did not develop meningitis while under our observation.

SUMMARY

Two fatal cases of torulosis of the central nervous system are described. One was a circumscribed cerebellar "toruloma," which was removed. The other was a diffuse meningo-encephalitis.

The clinical picture of torulosis of the central nervous system closely resembles that of tuberculosis of the central nervous system.

Penicillin, streptomycin, and various sulphonamides did not inhibit the growth of cultures of torula. Of the sulphonamides only soluthiazole had such an effect. Gentian violet exerted a considerable inhibitory effect on cultures.

We are indebted to Prof. D. S. Russell for allowing us to use her necropsy notes of case 1, and to Dr. J. T. Duncan for his mycological advice.

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DIABETIC KETOSIS

A COMPARISON OF RESULTS OF ORTHODOX AND INTENSIVE METHODS OF TREATMENT BASED ON 170 CONSECUTIVE CASES

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OUR purpose in presenting this paper is twofold: (1) to show that diabetic ketosis and coma can be satisfactorily treated with the facilities available in any ward side-room, and (2) to record the results of treatment in 170 cases, and the effects of changing from orthodox methods to the use of large quantities of intravenous fluid and insulin. We make no apology, therefore, that the results of elaborate biochemical investigations of this metabolic disorder are not included.

Fowler et al. (1940) suggested the routine use of immediate intravenous injections of large doses of soluble insulin, combined with subcutaneous injections of protamine zinc insulin and soluble insulin; 6 of 26 patients thus treated died. Root (1945) reported an improved mortality (1·6% in 123 consecutive cases), which he attributed to the increased amount of insulin given in the first three hours of treatment. Our present treatment has been evolved in accordance with this principle, and we believe that the results show a significant improvement.

DEFINITION OF DIABETIC COMA

In an attempt to simplify the management of these cases we have deliberately refrained from routine estimations of the alkali reserve of the blood. We therefore cannot state which of our cases falls within Joslin's (Joslin et al. 1940) biochemical definition of coma (CO_2-combining power of 20 vol. % or less). We have included only those cases which showed obvious and visible air-hunger on admission to hospital, for it can safely be claimed that at this stage ketosis has become urgent and that coma is impending. It seems that a clinical assessment is more accurate and helpful in deciding the severity of the ketosis than any chemical tests available at present. There is no doubt that a plasma CO_2-combining power below 20 vol. % is

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compatible with full consciousness and even absence of air-hunger, as is shown by the following case.

A woman of 30, with extremely acute and severe diabetes, came to the clinic by bus and walked into the consulting-room. The plasma CO_2-combining power was at that time 16 vol. %. With soluble insulin 30 units 4-hourly for 24 hours and a normal diet her urine was cleared of acetone, and at no time did her condition give rise to any anxiety.

On the other hand, in 20 cases of air-hunger in which the CO_2-combining power was estimated there has not been one above 20 vol. %. Blood-sugar levels bear no constant relation to the severity of the ketosis. Figures of 600 mg. per 100 ml. are not rare in patients without ketosis or untoward symptoms, whereas severe and obvious ketosis may be found with a blood-sugar as low as 350 mg. per 100 ml.

We restrict the term diabetic coma to cases in which the patient is unconscious from ketosis, and call the remainder diabetic ketosis. It is difficult to divide the cases into well-defined groups according to their severity, but three arbitrary stages have been used for the purpose of analysis: stage 1, drowsy but easily rousable; stage 2, rousable with difficulty; and stage 3, unconscious on admission.

ÆTIOLOGY

Diabetic coma is always due ultimately to lack of insulin. Clinically this is brought about in three possible ways: (1) excess of diet, (2) inadequate prescription or administration of insulin (e.g., a leaking syringe); and (3) intercurrent disease, usually infection, increasing the severity of the diabetic state. A history of diarrhœa and vomiting at the onset is surprisingly common, but no confirmatory evidence of infective gastro-enteritis is obtained, and constipation at the time of admission is the rule. In many cases there is no obvious reason for the loss of diabetic control.

DIAGNOSIS

We believe that the diagnosis of diabetic coma or ketosis, as defined above, is rarely difficult, and we certainly see no similarity between diabetic and hypoglycæmic coma. Only once in the period covered by these 170 cases has a doubtful diagnosis been made; here uræmia due to bilateral pyelonephritis in a diabetic patient presented a problem which was rapidly solved by testing the urine, which was found to contain only a trace of sugar.

The history of onset of the coma is of great value. Coma coming on suddenly—e.g., while the patient is walking along the street—is never diabetic, but may be hypoglycæmic. Diabetic coma may be rapid but not sudden in onset, and is heralded by symptoms evolving over hours. Of these symptoms the most prominent is usually vomiting; intense thirst and weakness are usual, and abdominal pain, general or mainly epigastric, may be so intense as to suggest an acute abdominal emergency.

The sign on which we place most reliance in the diagnosis of ketosis is air-hunger. This particular type of breathing (Kussmaul respiration) is highly characteristic and is only likely to be confused with that occurring in aspirin poisoning or in uræmia. The breathing in these three conditions is of the same type because of the presence of acidosis in all of them. A little practice soon enables one to detect the characteristic acetone odour in the breath of a patient with diabetic ketosis, but its presence is not invariable. The deep respiration of acidosis is quite unlike the rapid shallow respiration of pneumonia and heart-failure. Its depth is its most characteristic feature, though the rate is usually also moderately increased. In spite of the considerable increase of tidal air the patient seldom complains of dyspnœa. So constant is this that the presence of dyspnœa implies some other cause limiting the vital capacity. Not uncommonly, however, the hyperpnœa interferes with speaking. Long sentences may be interrupted by the respiratory movements.

The plantar reflex remains flexor with surprising constancy even in the terminal stage of coma. Indeed, the presence of an extensor response suggests a concomitant nervous lesion. In hypoglycæmia the extensor response appears early and may not revert until consciousness has been regained for some minutes.

The other signs of value in diagnosis are the result of dehydration and peripheral circulatory failure, notably the dry brown tongue, dry skin, sunken eyes, rapid thready pulse, and low blood-pressure.

The textbook tables of contrasting signs of diabetic and hypoglycæmic coma merely confuse the inexperienced by including inessential features. All too common is the student who examines the intraocular tension, decides (often wrongly) that it is low, and then cannot remember which type of coma this sign suggests.

CHEMICAL TESTS

We have reduced the number of chemical tests to the minimum necessary for treatment, and use only Benedict's for sugar and Gerhardt's and Rothera's for acetone bodies. These are carried out in a standard manner so that roughly quantitative results are obtained. Urine chlorides are estimated by Harvey's (1910) method.

A little care is required in the interpretation of urine tests with ferric chloride. Excretion products of aspirin and other substances yielding salicyluric acid give a deep violet colour, but this is quite different from the definitely reddish colour produced by acetone. These substances may also give a weak reduction both of Fehling's and of Benedict's solutions.

We have seldom had recourse to blood-sugar estimations in controlling the treatment of diabetic ketosis, and on those occasions have used the Zeiss colorimeter. This estimation is carried out by using 0·2 ml. of blood, which can be obtained by finger puncture, and a result is available in 15 minutes. A series of controlled estimations by the Hagedorn and Jensen method shows that the error is ± 10%, which is adequate for clinical purposes.

OUTLINE OF TREATMENT

(1) As soon as the diagnosis is established, an initial dose of soluble insulin 200–400 units is given intravenously. The exact dosage depends on a clinical assessment of the severity of the case. Broadly speaking, we administer 200 units to cases in stage 1, 300 units to those in stage 2, and 400 units to those in stage 3 (see above).

(2) As rapidly as possible an intravenous drip is set up, and within the first 15 minutes a pint of normal saline is infused. A second pint is given in the second 15–30 minutes, and perhaps a third pint at the same rate. Thereafter a solution of 5% glucose in physiological saline solution is administered, usually at the rate of one pint hourly.

(3) As soon as the intravenous drip has been set up, a urethral catheter is passed and the bladder emptied. Thereafter the bladder is emptied every 30 minutes. Each specimen of urine collected is measured and tested with Benedict's solution and ferric chloride. The results are charted on a simple form by a system of plus signs. Specimens are also tested frequently for urinary chlorides.

(4) Further soluble insulin in doses of 50 units is injected into the drip tubing every 30 minutes until the urine becomes free of acetone bodies by the Gerhardt test.

(5) Occasionally during treatment trouble is experienced through persistent vomiting. We have not found routine gastric lavage necessary, and it carries the risk of aspiration pneumonia. The tendency to vomit disappears rapidly with the abolition of ketosis and we

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prefer to treat this energetically and to restrict oral fluid to sips of water for relief of thirst for a few hours. However, where vomiting is persistent, we pass a Ryle's tube and aspirate the stomach contents at regular intervals. Occasionally, acute dilatation of the stomach is seen in diabetic ketosis and, as pointed out by Marriott (1947), this may be the result of chloride depletion. This condition is an absolute indication for gastric aspiration. Experience has taught us that the intravenous drip should be kept running after the disappearance of ketosis until further vomiting is unlikely, particularly in view of the frequency of chloride depletion. It may be discontinued when the patient is again able and willing to take glucose fluids by mouth.

RATIONALE OF TREATMENT

The immediate objects in treatment of ketosis are: (1) the abolition of ketosis, (2) rehydration, and (3) restoration of chloride.

The presence of dehydration needs no emphasis, but the quantity of fluid required is surprising. We estimated this in a boy of 6 st. 11½ lb. (43·3 kg.). The plasma volume was 1700 ml. by Evans's method, and the hæmatocrit 57%. This represents a blood volume of 2610 ml., a reduction of 810 ml. of the blood volume expected for his weight. On Marriott's assumption that the plasma loss may be multiplied by 6 to give the total extracellular fluid loss, this boy had an extracellular fluid deficit of 4·8 litres, or 8½ pints.

The presence of chloride depletion, too, is not surprising. In the hours or days preceding the onset of ketosis, profuse diuresis has led to considerable loss of water and chlorides. Resulting anorexia leads to cessation of chloride intake. With the onset of ketosis, chloride depletion is increased by vomiting, and the excretion of ketone bodies in the urine carries away further quantities of fixed base, especially sodium (Peters et al. 1933). Even in the absence of vomiting it is the rule for the urinary chloride to be of the order of 0·5–1·0 g. per litre on admission to hospital. Marriott has estimated that a urinary chloride so low represents a probable deficit of at least 4 litres, or 7 pints, of isotonic saline solution in a man weighing 70 kg. Vomiting produces a fall of plasma chloride, and Franks et al. (1947) record an average plasma chloride of 494 mg. per 100 ml. in 24 severe cases of ketosis.

Choice of Intravenous Fluids.—We prefer to start treatment with 3 or 4 pints of physiological saline solution intravenously in the first 1½–2 hours along with large doses of insulin, and after this quantity to change to 5% glucose in physiological saline, one pint hourly. Root (1945) believes that there is ample glucose in the tissues of the patient with diabetic coma, and that no further glucose is required. He even believes that further glucose may do harm, and cites experimental evidence that it may damage the liver (Astwood et al. 1942) and may produce anuria (Allen 1938). On clinical grounds we have not been convinced that this is a crucial point, and are more inclined to agree with the observations of Franks et al. (1947), who point out that the following chain of events is set up by the early administration of glucose: glucose administration→hyperglycæmia→excessive glycosuria→polyuria. These workers treated two groups of cases with dextrose or with saline solution. The water intake of the dextrose group was only slightly greater than that of the saline group, but the urinary output was nearly four times as great. They attribute this to an elevenfold increase in the glucose output. We have recorded the urine outputs in several cases and confirm the polyuria resulting from early administration of glucose. This delays restoration of the blood volume and perpetuates peripheral circulatory failure and extracellular dehydration. Accordingly we prefer to administer physiological saline solution at first, and to change later to 5% glucose in saline to prevent the disappearance of glycosuria before the ketosis has been abolished. This is a real danger, since the carbohydrate store may be almost completely exhausted and the circulating sugar may represent the greater part of the carbohydrate reserve.

Method of Insulin Administration.—It is generally accepted that small doses of insulin at short intervals are more effective than larger doses infrequently (Joslin et al. 1940). Our only criticism of this principle is that the small doses are made too small. To end as rapidly as possible the diuresis due to hyperglycæmia and heavy glycosuria we start with an initial dose of soluble insulin 200–400 units intravenously. This is followed by 50 units every 30 minutes into the drip tubing until the urine becomes free of ketone bodies to ferric chloride or until air-hunger has disappeared. With the routine of intravenous fluids already described we have never seen the glycosuria end before the disappearance of ketosis. We believe that the administration of subcutaneous soluble insulin in the treatment of ketosis is the cause of sudden transition from hyperglycæmia to hypoglycæmia. In the presence of peripheral circulatory failure absorption of insulin given subcutaneously is at first poor, but enough is absorbed to terminate the profuse diuresis and to restore the circulatory volume. As soon as this is restored, further absorption is rapid from all injection sites or "depots." The change to hypoglycæmia is then rapid and may be unsuspected, without consciousness being regained. Intravenous insulin is devoid of this danger, since each injection produces its own measurable effect. The rapidity with which ketosis is abolished with intravenous insulin has the further advantage that the period of anxiety for the patient's welfare, and thus for repeated close observation, is greatly reduced.

TABLE I—USUAL DOSAGE OF INSULIN AND DURATION OF KETOSIS

—	Stage 1	Stage 2	Stage 3
No. of cases	8	12	4
Ave. dose of insulin required to abolish ketosis (units)	265	726	870
Range of insulin dosage (units)	140–500	250–1400	500–1400
Ave. duration of ketosis (hours)	15·4	11·4	17·6
Range of duration of ketosis (hours)	7–23	4–27	14–27

QUANTITY OF INSULIN REQUIRED AND RATE OF RECOVERY

Table I shows the average quantities of insulin required, the range of dosage, the average duration of ketosis, and the range of its duration in 24 representative cases.

Table II compares the average quantities of insulin required, the range of dosage, the average duration of ketosis, and the range of its duration in stage-2 cases treated by different methods of insulin administration.

No comparison is possible of results by different methods of administration in stage-1 and stage-3 cases, since almost all stage-1 cases were treated by hypodermic, and stage-3 cases by intravenous, injections.

RETURN TO DIET AND ROUTINE INSULIN DOSAGE

For some hours after the disappearance of ketosis the patient's appetite remains poor, and glucose and fluids are the most that can be taken by mouth. Usually the anorexia of this stage is the result of chloride depletion, readily recognised if the urinary chloride is estimated. Other clinical features of chloride depletion may be evident: apathy, drowsiness, and stupor may persist in spite of the disappearance of ketosis—a state of affairs recognised by Peters et al. (1933). The solution

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TABLE II—DOSAGE OF INSULIN AND DURATION OF KETOSIS IN DIFFERENT METHODS OF GIVING INSULIN

Method of insulin administration	Hypodermic	Intramuscular	Intravenous
Ave. dose of insulin required to abolish ketosis (units)	250	480	656
Range of insulin dosage (units) ..	140–530	430–530	350–1400
Ave. duration of ketosis (hours) ..	12·0	11·5	7·46
Range of duration of ketosis (hours)	8–15	8–15	4–11·5

of 5% glucose in physiological saline may be continued intravenously, and is not unpalatable for oral administration. To cover this period we aim to give a third of a pint of 5% glucose in physiological saline solution hourly for 6–8 hours, and a dose of soluble insulin 30–40 units subcutaneously. After this time, with restoration of the lost chlorides, appetite returns, and we put the patient back on a light diet, prescribed in terms of "rations." Each ration represents 10 g. of carbohydrate, and may also include unspecified quantities of protein, fat, and chloride. An average diet for an adult would be 180–200 g. of carbohydrate. Usually the patient can resume normal diet 24 hours after the disappearance of ketosis, provided chloride depletion has been overcome.

Where a known diabetic patient has been rescued from ketosis, the insulin requirements are increased for a few days and then usually return to normal (where this was previously satisfactory).

RESULTS

Root (1945) gives no detailed analysis of the clinical features of his cases, and the same course has been followed in this paper, since it seems probable that any large series will contain a similar number of mild and severe cases, and that the ætiological factors will show the same variety.

Table III shows the mortality in 170 cases of diabetic ketosis treated at the General Hospital, Birmingham. These have been divided primarily into two groups: group 1 from January, 1943, to February, 1946, during which time treatment was in the main orthodox; and group 2 from February, 1946, to June, 1948, during which the more intensive treatment described above was used. Towards the end of this period considerably larger doses of insulin were introduced, and group 2a consists of the last 30 cases in the second group. The average insulin dose in the first 3 hours, as shown in table III, indicates the extent of the increase of insulin dosage. Comparison of these groups shows the striking improvement of mortality that can be achieved. The possibility that penicillin may have contributed to this improvement has not been overlooked. This drug became generally available early in 1945, and there is no doubt that in a few of the later cases, associated with severe infection, it has saved life. But such cases are a very small minority, since sulphonamides were used throughout the period under review.

TABLE III—MORTALITY IN 170 CASES OF DIABETIC KETOSIS

—	Group 1 *	Group 2 †	Group 2a ‡
No. of cases	80	90	30
Over-all mortality	23 = 28·7%	9 = 10·0%	2 = 6·6%
Average insulin dosage in first 3 hr. after admission	107·5	220	316
Deaths from uncontrolled ketosis	12 = 15·0%	6 = 6·6%	1 = 3·3%
Deaths from causes other than uncontrolled ketosis	11 = 12·2%	3 = 3·3%	1 = 3·3%

* Period January, 1943, to February, 1946.
† Period February, 1946, to June, 1948.
‡ Period August, 1947, to June, 1948, being the last 30 consecutive cases of group 2.

SUMMARY

The treatment of diabetic ketosis by the intravenous administration of large doses of insulin and physiological saline solution is described.

In 170 cases the mortality was reduced from 28·7% to 6·6%; this improvement is attributed to the increased intensity of the treatment.

The importance of the recognition of chloride depletion and its rectification are emphasised.

We should like to thank Dr. Robert Gaddie for continuous helpful criticism and advice.

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TOXIC EFFECTS OF TRIDIONE

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IT is generally agreed that 'Tridione' (3,5,5-trimethyloxazolidine-2,4-dione) is one of the most effective drugs used in the treatment of petit mal. Though the possibility of toxic effects is well recognised, few such cases have been reported, and the impression gained from published accounts is that, though minor toxic reactions are common, serious reactions are rare.

We describe here the toxic complications that developed in the small series of cases treated in the Sheffield Children's Hospital. These reactions have been so severe that we feel that the dangers of tridione may outweigh its therapeutic value.

Tridione has been used for many years in intermittent dosage as an analgesic (Erlenmyer 1938, Luton et al. 1941) with no apparent serious complications. Everett and Richards (1944) demonstrated its anticonvulsant effect on convulsions produced with leptazol and electrical stimuli in animals. Since then the effect of tridione in about 400 cases of epilepsy has been reported. Lennox (1945, 1946a and b, 1947) recorded the largest series in four articles which apparently cover the same cases. He described 245 cases, including 166 of petit mal; of these 31% were rendered free from fits, 32% had less than a quarter of the previous number of fits, 20% showed some improvement, 13% were unchanged, and 4% became worse. He noted photophobia in 31%, skin rashes in 14%, and other symptoms. He observed one case of aplastic anæmia (Harrison et al. 1946), which developed after eight months' treatment with tridione, and he stated that he had heard of 4 cases which had developed this complication.

Davis and Lennox (1947) reported the effect of tridione on the blood-count in 127 patients. In 20 a count was done before treatment was started, and an average of less than three counts was done on each patient. These workers noted that a neutropenia of under 1600 per c.mm. developed in 6·3% of the cases.

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The neutropenia was of gradual onset, and they recommended monthly blood-counts and withdrawal of tridione if the neutrophil-count fell below 1600 per c.mm. They observed no fall in platelets or red blood-cells.

Two further cases of fatal aplastic anæmia have been reported. Mackay and Gottstein (1946) described one which developed after ten months' treatment with tridione; and Braithwaite (1948) one in which urticaria developed on the twenty-fifth day, and a fatal anæmia after fifty-one days, of treatment with tridione. THE LANCET (1947) mentioned a fatality due to aplastic anæmia occurring in this country after treatment with tridione.

Greaves (1946) observed a sudden granulopenia in a case treated for eighteen days with tridione. The blood returned rapidly to normal when the treatment was stopped, but the granulopenia recurred when tridione was given again.

Several small series of cases have been reported with no toxic effects—DeJong (1945, 1946) 60 cases, Perlstein and Andelman (1946) 75 cases, and Butter (1948) 23 cases—but no hæmatological or urological investigations were mentioned.

Barnett et al. (1948) reported what appears to be the only case of renal complication due to tridione:

A girl, aged 16, developed massive albuminuria and œdema after eight months' continuous tridione therapy. The drug was stopped, and, after five weeks' rest in bed and a low-salt and low-fluid diet, her blood biochemistry was normal, her œdema and albuminuria subsided, and her fits recurred. Renal function was then normal. Tridione was again given, and two months later the patient had generalised œdema and a low blood-albumin level. Again the condition subsided when tridione was stopped. Clinical and laboratory findings once more returned to normal in four and a half weeks, and the fits recurred. Because of frequent attacks of petit mal tridione was once more started, and two months later, for the third time, the patient had generalised œdema, a low serum-albumin level, and high blood-cholesterol and blood-urea levels. It took five and a half weeks, after tridione had been stopped, for the œdema to subside and for the biochemical findings to return to normal. Phenobarbitone was substituted for tridione, and five months later there had been no recurrence of the œdema. Hæmaturia developed in the two later attacks.

The striking relation between the administration of tridione and the nephrotic state in this case could hardly have been fortuitous.

CASE-RECORDS

The present series of 10 cases (table I) includes all the children who have been treated with tridione at the Sheffield Children's Hospital.

Case 1.—A girl, aged 6¾ years, was having four attacks of petit mal a day. She was treated with tridione 0·3 g. b.d. and the attacks ceased, but within a fortnight the neutrophil count fell to 400 per c.mm. Tridione was stopped, and the neutrophil-count returned to normal within three weeks, and the fits recurred.

Case 2.—A girl, aged 11, was having twelve attacks a day. Tridione 0·3 g. b.d. reduced the attacks to three a day. Three weeks later a massive urticaria developed, tridione was withdrawn, and the attacks returned. After an interval of nine months tridione was again given, in a dose of 0·3 g. four times daily, this time with 'Benadryl' 0·25 g. b.d. The fits ceased entirely, and the child has remained symptom-free for two months, with no urticaria or neutropenia.

Cases 3 and 4.—A boy, aged 10, and a girl, aged 8, had both petit mal and grand mal. They were treated with tridione 0·3 g. t.d. for two weeks and two months respectively. The dose was then increased, but in neither case was the incidence of the fits reduced, and the drug was stopped as being of no value.

Case 5.—A boy, aged 7, had both petit mal and grand mal. For a month the incidence of attacks of petit mal decreased under treatment with tridione, but then the original intensity of attacks recurred and was unaffected by an increased dosage. Treatment with tridione was therefore stopped. There was no further increase in fits.

Case 6.—A girl, aged 13, had both petit mal and grand mal. Tridione 0·3 g. b.d. abolished the petit mal but did not affect the grand mal. After five months the tridione was stopped and the petit mal did not recur. The grand mal has continued and the patient is receiving phenobarbitone.

Case 7.—A boy, aged 12, had twelve attacks of petit mal a day. These attacks were completely stopped with tridione 0·3 g. four times a day. The patient had been treated for thirteen months, when he developed a leucopenia, with 1500 neutrophils per c.mm. After the tridione had been stopped, the number of neutrophils fell further for two weeks and then returned to normal. The petit mal returned after the withdrawal of tridione.

TABLE I—ANALYSIS OF CASES OF PETIT MAL TREATED WITH TRIDIONE

Case no.	Age (years)	Sex	Form of epilepsy	Average no. of daily attacks of petit mal		Approx. daily dose (g.)	Length of treatment	Toxic effects	Remarks
				Before	After				
1	6¾	F	Petit mal	4	0	0·6	2 weeks	Neutropenia	Neutrophil-count fell to 400 per c.mm.; drug stopped and fits returned; count returned to normal in 5 days
2	11	F	,,	12	3	1·2	3 weeks	Urticaria	Normal white-cell count; after 9 months was again put on tridione and benadryl 0·25 g., fit-free for 2 mos., no toxic complications; still on the drug
3	10	M	Grand mal & petit mal	6	6	1·2	2 weeks	None	No therapeutic response
4	8	F	,,	4	4	0·9	2 mos.	,,	No therapeutic response
5	7	M	,,	5–10	5–10	1·2	2 mos.	,,	No therapeutic response
6	13	F	,,	4–5	0	0·6	5 mos.	,,	Drug stopped; no recurrence of petit mal; grand mal controlled with phenobarbitone
7	12	M	Petit mal	12	0	1·2	13 mos.	Neutropenia	Leucopenia; neutrophils 1500 per c.mm.; fall continued for 2 weeks after cessation of tridione and then white-cell count returned to normal; petit mal returned
8	13	F	,,	12	0	0·9	14 mos.	None	Drug gradually reduced and stopped after 14 mos.; no recurrence of fits
9	9½	M	,,	12	0	1·8	11 mos.	Complete depression of bone marrow	See case-record
10	8	M	,,	60	6	1·8	11 mos.	Died	,,

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Case 8.—A girl, aged 13, was having twelve attacks of petit mal a day. Tridione 0·3 g. t.d. stopped the fits, and the dose was gradually reduced to 0·3 g. twice weekly. After fourteen months on this dosage, the tridione was stopped and the petit mal did not recur.

Case 9.—A boy, aged 9½ (table II), had attacks of petit mal which had started when he was 7 years old and were not controlled with phenobarbitone and bromides. Tridione treatment was started in April, 1947, and the number of attacks immediately lessened. In January, 1948, the neutrophil-count fell below 2000 per c.mm., but in view of the child's good general condition the drug was continued until March 5, when the neutrophils had fallen to 700 per c.mm. Despite the fact that tridione was stopped, the neutrophil-count fell steadily to less than 100 per c.mm. during the second week in April. On April 4, a sternal-marrow smear showed a profound depression of all the granular series, and no megakaryocytes were seen in the films. The platelets in the peripheral blood were fewer than 500 per c.mm.

TABLE II—MARROW AND PERIPHERAL BLOOD-COUNTS IN CASE 9

	Date (1948)				
	April 3	April 19	May 11	May 25	June 2
Marrow:					
Granular series (neutrophils, &c.) (%)	3·8	23·8	26·4	41·6	35·2
Lymphocytes (%)	63·8	58·0	53·4	41·0	22·8
Red-cell series (%)	20·2	0·6	11·0	9·6	41·4
Megakaryocytes (%)	< 0·001	<0·001	0·2	0·6	0·2
Peripheral Blood:					
Total leucocytes per c.mm.	2500	4500	5500	6000	6000
Neutrophils per c.mm.	250	800	1300	2500	2800
Red cells (millions per c.mm.)	3·3	4·4	2·1	3·4	3·7
Platelets per c.mm.	>500	9000	>500	34,000	160,000

On April 8 the patient had a small epistaxis, and numerous petechiæ appeared on his trunk. Fresh blood (2 pints) was then given. This appeared to control the purpura, but the platelets in the peripheral blood were often too few to count. The marrow on April 19 showed that the depression of the neutrophils had been superseded by a severe depression of the red-cell precursors (table II). At this time the patient was very well and having no attacks of petit mal. However, though the number of leucocytes in the peripheral blood was rising, the red-cell count, despite the transfusion, continued to fall. Bone-marrow biopsy at this time showed a return of megakaryocytes and the granular series recovering well before the red cells. Table II shows that the number of red-cell precursors remained about 10% of the marrow cells until June 2, when it rose to about 40%. The attacks of petit mal, which had stopped when the epistaxis occurred, returned again with increased frequency at the beginning of June.

Case 10.—A boy, aged 8, was first admitted in March, 1947, with a history of up to sixty attacks of petit mal a day, which appear to have followed a major seizure two years previously. The petit mal attacks were observed in the ward, and the administration of tridione almost completely controlled them. During his stay in hospital the routine ward-tested specimens of urine and a single laboratory specimen showed no abnormality. He was discharged on tridione 0·3 g. five times daily. He was watched in the outpatient department, during which time he was quite fit but having about six attacks of petit mal a day.

In June, about four months after the start of tridione treatment, the child rapidly developed severe œdema and within six days required a paracentesis abdominis. The urine at that time contained up to 10 g. of albumin per litre. A few granular casts were present and a normal number of red cells. Total serum-protein was 4 g. per 100 ml., blood-urea 190 mg. per 100 ml., and serum-cholesterol 400 g. per 100 ml. There was no anæmia or neutropenia. The possibility that the nephrotic state was due to a toxic effect of the tridione was considered, and the drug was withdrawn immediately. After six weeks there was no improvement in the nephrotic state, and attacks of petit mal were occurring with increased frequency. Tridione was then given for eleven days. After a further period of about five weeks off the drug, tridione was again given, in a dose of 0·6 g. daily until the child's death.

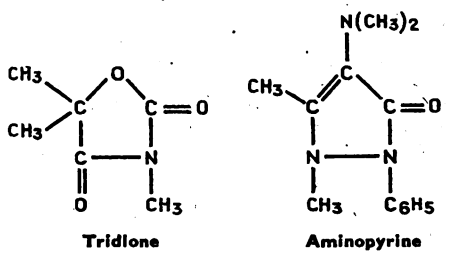
Despite low-fluid and low-sodium diet and rest in bed the blood-urea level remained high—151 mg. per 100 ml. on July 25; 117 mg. on July 30; and 73 mg. on Aug. 28—and the serum-cholesterol remained at the same level as on admission. The serum-protein level never rose above 4 g. per 100 ml. The urinary albumin level was persistently above 0·5 g. per 100 ml., and cellular casts were never seen. The urine contained less than 5 red cells per high-power field of the centrifuged deposit, except on one occasion when 10 were present. The Addis count (Aug. 9, 1947) showed 600,000 red cells in twelve hours. The urinary output was 6–20 oz. a day (average 15 oz.), and the specific gravity was always 1020 or more. Paracentesis abdominis was required at about ten-day intervals, and on each occasion 6–8 pints of fluid was withdrawn.

The general condition gradually deteriorated during the next five months. The child was taken home in February, 1948, and died within a few days. No necropsy.

DISCUSSION

Of 10 cases of petit mal treated with tridione, in 3 (nos. 3, 4, and 5) the drug was stopped because it did not control the attacks. The attacks were much reduced in the remaining 7 cases (1, 2, 6, 7, 8, 9, and 10). In 3 of these cases (2, 6, and 8) there were no toxic complications during treatment with tridione. In 3 others (1, 7, and 9) tridione had to be stopped because of neutropenia. In case 1 neutropenia developed almost immediately, but the neutrophil count rapidly returned to normal when tridione was discontinued. Neutropenia did not occur in the 2 other cases (7 and 9) until treatment with tridione had lasted more than ten months, and the leucocyte-count fell still further for several weeks after tridione had been stopped. Bone-marrow biopsy in case 9 was important, for it showed that tridione had a toxic effect on all the elements of the marrow. The megakaryocytes were depressed either after or during the depression of the granular series, and the erythroid series were still almost completely depressed by the time the other cells were regenerating. The remaining patient (case 10) in whom tridione was effective in reducing petit mal developed a nephrotic syndrome after four months' treatment. It is difficult to assess the relation between the use of tridione and this syndrome, but in view of the case reported by Barnett et al. (1948) there is little doubt that such a relation exists. The rapid development of massive œdema, low serum-protein level, high blood-urea level, and little cytological change in the urine in our case exactly parallels the syndrome they describe.

The toxic effect of tridione on the bone-marrow is almost certainly related to the presence of a pentagonal ring structure closely resembling that of the aminopyrine group of drugs:



We cannot explain why tridione should cause a nephrotic state.

SUMMARY

Of 10 cases of petit mal, tridione reduced the frequency of fits in 7.

Of 4 children treated with tridione for more than six months, 2 showed a severe depression of the neutrophil count.

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After thirteen months' treatment 1 child developed purpura and a severe depression of all elements of the bone-marrow. After transfusion he recovered. Another child, after four months' treatment, developed a nephrotic condition and died.

In this short series the toxic complications of tridione proved more dangerous than the disease it is used to treat.

Our thanks are due to Prof. R. S. Illingworth, Prof. E. J. Wayne, and Dr. T. Colver for help and advice.

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HYPERTENSION FOLLOWING RENAL INFARCTION

JOHN WAINWRIGHT
M.B. Sheff.

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RENAL ischæmia is now a well-known cause of hypertension in man and animals, but there are few recorded cases where the onset of hypertension in man can with certainty be related to renal infarction. The following case is reported in detail since, before accepting renal infarction as the cause of hypertension, one must be certain that the hypertension was not pre-existent but temporarily in abeyance owing to infection or cardiac failure.

A licensed broker, aged 47, was admitted as an urgent case to the Manchester Royal Infirmary under the care of Dr. A. H. Holmes on May 4, 1947. He had four years' history of dyspnœa, palpitations, hæmoptysis, and œdema of the ankles. He had had diphtheria in childhood and appendicitis at 20.

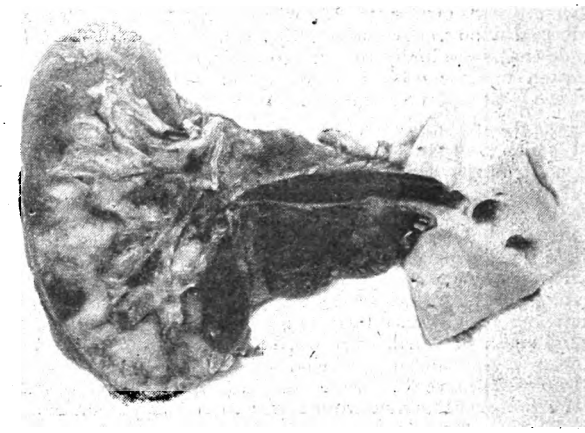
On examination the patient was orthopnœic, cyanosed, emaciated (weight 40 kg.), and distressed. The neck veins were engorged and the heart was enlarged; auricular fibrillation and systolic and diastolic apical bruits were present. The liver was enlarged and tender, and numerous râles were audible at the bases of both lungs. There was œdema of the ankles. The blood-pressure then and later was 110/80 mm. Hg. Radiological and cardiographic examination confirmed a diagnosis of chronic rheumatic heart disease with mitral stenosis, auricular fibrillation, and congestive heart-failure. Digitalis was given, and with rest the œdema and congestion gradually subsided. The patient went home on June 9, 1947, against medical advice.

He was readmitted on Aug. 19, 1947, with congestive heart-failure, and the physical signs were as before. His blood-pressure was still 110/80 mm. Hg, and blood-urea 20 mg. per 100 ml. He was again treated with digitalis.

Aug. 26: the patient complained of pain and tenderness in the right loin, with pallor, sweating, nausea, and vomiting, and the symptoms suggested renal colic. No red blood-cells were found in the urine. His temperature rose to 100·6°F, though earlier and later he was apyrexial.

Sept. 2: the right loin and hypochondrium were extremely tender, and the œdema and congestion had increased. Blood-pressure 140/80 mm. Hg.

Sept. 9: the liver was now enlarged to three finger-breadths below the costal margin. The systolic blood-pressure was 150 mm. Hg; the diastolic pressure could not be recorded accurately.



Right kidney showing thrombus in renal artery and irregular infarction of kidney.

Sept. 16: the patient had attacks of cardiac asthma and coughed up abundant sputum. The œdema was rapidly increasing and his condition deteriorating. Blood-pressure 210/100 mm. Hg.

Sept. 23: the patient died with symptoms of left ventricular failure.

Necropsy Findings.—The right kidney (100 g.) was smaller than the left. An irregular pale infarct occupied most of the kidney. The right renal artery was completely occluded by a dark red thrombus, extending from its aortic orifice to its bifurcation, and firmly adherent to the wall. The left kidney (200 g.) was swollen, with normal architecture, and the medulla was congested. The aorta and renal arteries showed early atheroma. The heart (490 g.) showed right ventricular hypertrophy. The auricles were dilated but free from thrombi. The mitral valve was slit-shaped and partly calcified. The aortic cusps were sclerosed, and calcified plaques were present. The left ventricle was dilated. The coronary arteries were healthy. The right pleural cavity contained about 800 ml. of straw-coloured fluid, and the lower lobe of the right lung was collapsed. Both lungs (500 g.) were greatly congested and œdematous, and the pulmonary arteries showed extensive atheroma. The liver (1100 g.) showed chronic venous congestion, and the spleen (200 g.) was firm and dark red.

Histology.—The right kidney showed irregular areas of complete necrosis with early organisation. A few dilated vessels containing fresh blood were present in the infarcted zone. The intermediate areas showed atrophy and fatty degeneration of the tubular and glomerular epithelium and intense vascular congestion. The right renal artery showed early atheroma and organisation of the thrombus. In the left kidney there were subcapsular foci of atrophied tubules, fibrosis, and lymphocytic infiltration. Neither kidney showed any changes in the intimate vasculature. The lung showed masses of heart-failure cells in the alveoli, with congestion and œdema; there were scattered miliary foci of fibrosis, with collections of foreign-body giant cells and granules of free iron.

DISCUSSION

The clinical and pathological findings indicate embolic occlusion of the right renal artery, with massive renal infarction and the development of hypertension first noted after seven days. The possibility of a primary thrombosis of the renal artery cannot be entirely excluded on pathological grounds, but the absence of gross disease of the renal artery renders this unlikely. The cardinal signs of leucocytosis and hæmaturia in addition to pyrexia were not found (hæmaturia may be absent if no urine is secreted by the infarcted kidney). A blood-count was not made at this time, since the condition was diagnosed only at necropsy.

Few examples of hypertension following renal infarction confirmed at necropsy have been reported. Fishberg (1942) reported 3 cases of mitral stenosis in which hypertension, persisting until death, developed at various intervals after embolism of a renal artery. Prinzmetal et al. (1942) recorded a similar case in a

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patient with chronic rheumatic heart disease; the perfusate from the partially infarcted kidney removed immediately after death contained a pressor substance as found in the experimental ischæmic kidney. Yuile (1944) reported 2 cases of thrombotic occlusion of the renal artery in which hypertension developed; in both the kidney with the occluded renal artery was free from arteriolar changes, whereas the opposite kidney showed much hyalinisation of arterioles.

Clinical cases of hypertension following renal infarction are also few. Fishberg (1942) reported a case of transient hypertension following symptoms of embolism of a renal artery after myocardial infarction. Ben-Asher (1945) has described transient hypertension following clinical renal infarction in a patient with mitral stenosis and auricular fibrillation who had been under observation for many years. There were hæmaturia, pyrexia, and leucocytosis, and an excretory pyelogram gave no picture on the right side though a retrograde pyelogram was normal. The blood-pressure rose to 180/106 mm. Hg and gradually subsided after three weeks, when a further excretory pyelogram showed normal function of both kidneys. In a clinical review Wolffe (1943) mentioned the rise in blood-pressure which occasionally develops in severe cases of thrombosis of a renal artery.

Loomis (1946) has found that renal infarction following arterial ligation in rats produces hypertension, and considers that the pressor agent is formed by the absorption of the necrotic renal tissue. Fishberg (1942), on the other hand, considers that embolism of a renal artery is a natural example of the Goldblatt clamp, and that the hypertension is due to relative ischæmia of still functioning renal tissue. The experiment of Prinzmetal et al. (1942) supports the view that the pressor agent is renin. In the published cases the infarction has always been partial, and in my case the kidney tissue between the infarcted areas, though congested, showed well-marked epithelial atrophy, suggesting partial ischæmia. With bilateral renal infarction, where the renal vein was intact, hypertension developed in 70% of the rats in the first week. Similarly in the rabbit the blood-pressure may rise three days after ligation of a renal artery (personal observation). In the published cases in man hypertension developed as early as the third day after clinical emolism.

Fishberg (1942) discusses the rarity of hypertension in man after embolism of a renal artery. He comments on the individual predisposition to hypertension, the general condition of the patient in that fever may militate against its development, and the ratio of partially ischæmic but still functioning renal tissue to the total mass of functioning renal tissue. The amount of functioning renal tissue is of great importance in the rat, where Loomis (1946) found that the hypertension was more severe the smaller the amount of residual functioning renal tissue, and that this factor was of more importance than the extent of the infarction. Possibly in cardiac failure, which is common to most of the recorded cases, the chronic venous congestion of the kidney, with local anoxia, renders the non-infarcted kidney less able to destroy or neutralise the pressor substance.

Since the present patient was under observation for four months with a normal blood-pressure, and since he rapidly developed hypertension after symptoms of renal infarction which at necropsy was shown to be of recent origin, this case is a further example of a renal cause of of hypertension in man. It further emphasises that in man a unilateral renal lesion can cause hypertension.

SUMMARY

A case of hypertension following embolism of a renal artery with massive infarction of the kidney is reported.

The patient had mitral stenosis with auricular fibrillation and congestive heart-failure.

The few reported cases are briefly reviewed in the light of experimental studies of renal infarction.

I wish to thank Dr. Holmes for permission to publish this case, Prof. S. L. Baker for helpful criticism, and Mr. F. Ward for the photograph.

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Reviews of Books

The Dawn of Scottish Social Welfare

THOMAS FERGUSON, M.D., F.R.C.P.E., professor of public health, University of Glasgow. Edinburgh: Nelson & Sons. 1948. Pp. 320. 21*s*.

THE excellent history of the Kingdom of Scotland has been written by many authors of note, and its social conditions have been carefully investigated by Graham and others. Professor Ferguson's new book fills in one gap in the story by describing the main problems of health and social welfare from medieval times up to the middle of the 19th century. Thus far he brings together in a readable form much information that has been scattered in monographs and official reports; but he takes a further step in showing how these problems were tackled as they arose, and in this way makes an important contribution to our understanding of social medicine. He takes as his framework the four main problems: the control of epidemic disease, the improvement of environment, the reaction to poverty, and the provision of medical care. On all counts the hardships of the Scots were accentuated by the recurring periods of famine, and by the poor quality of stock and soil. In medieval times housing troubles were short-lived: "For though the Englysshe men brinne our housis we axe but thre deyes to make them agayne, if we may gete four or fyve stakes and bowes to cover them." Unhappily, in the 19th century the gaunt tenements were built all too solidly, and they still defy the housing reformer. The sections dealing with relief of the poor are written in a fresh and interesting way, and offer many comparisons of value to the English reader; it will comfort him to note that Littlejohn, as M.O.H. of Edinburgh, pleaded for the union of parochial boards in order that, laying aside all rivalry and jealousy, they should combine to erect one good poorhouse in a healthy situation, away from the centre of the city. He will also be amused to find that even the remote inspectors of the poor were "too fond of technicalities."

Professor Ferguson can always be guaranteed to make his subject attractive; he writes with accuracy and discernment and his pawky wit pervades the book.

Crystalline Enzymes

(2nd ed.) JOHN H. NORTHROP; MOSES KUNITZ; ROGER M. HERRIOTT. New York: Columbia University Press. London: Oxford University Press. 1948. Pp. 352. 42*s*.

DURING the nine years that have elapsed since the first edition of this book was published, the number of enzymes that have been crystallised has grown from 10 to over 30, and it can be said with more confidence that the crystals are composed of pure proteins and that the pure proteins really are the enzymes. The book gives a detailed account of the preparation and properties of about a dozen enzymes, enzyme precursors, and inhibitors. Full practical details of the preparations are given in the appendix, and particular attention is paid to the more recently investigated criteria by which the purity of proteins can be established. The book is beautifully produced, with over a hundred illustrations, including phase-rule solubility curves, and some fine photographs of crystals prepared in the authors' laboratory. There is more in the text than the title suggests: thus the general features of enzymic catalysis are discussed, and crystalline diphtheria antitoxin, bacterio-

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phage, and the action of mustard gas on enzymes and some other proteins are reviewed. If viruses and antibodies are enzymes, or are related to them, and if they are all proteins, there is every justification for the interesting final chapter on the biological synthesis of proteins. If little in this volume seems to bear directly on medicine now, much of it must come in time to be accepted as fundamental.

The Childless Marriage

E. F. GRIFFITH, M.R.C.S. London: Methuen. 1948. Pp. 206. 8s. 6d.

Dr. Griffith's book is a revised version of his original *Childless Family*. It will be of use to lay and social workers and members of the nursing profession, and to doctors making their first approach to the subject of human infertility. The ground is adequately covered; but there are some rather tiresome inaccuracies, and the illustrations, apart from the salpingograms which are excellent, are rather poor. Some interesting case-histories and a long and careful discussion of the indications for, and the ethics and social implications of, artificial insemination are among the more valuable features of the book.

The Leptospiroses

P. H. VAN THIEL, professor of parasitology of the University and the Institute of Tropical Medicine at Leyden. Leyden: Universitaire Pers. 1948. Pp. 231. Fl. 4.90.

Professor van Thiel describes and reviews a mass of data about leptospirosis in man and animals. Much of the original work was done in Holland, Denmark, and the Dutch East Indies, and has not been readily accessible to English readers. The first half of the book deals with leptospiræ in general.

He believes that leptospiræ are more closely related to protozoa than to bacteria, and classifies Leptospira, along with Borrelia and Treponema, as subgenera of the genus Spirochæta. This is at variance with the 1948 edition of Bergey's *Manual of Determinative Bacteriology*, which accords Leptospira generic status in the family Treponemaciæ. On the question whether all leptospiræ should be included in a single species he accepts the "mitigated pluralistic view" adopted by Schüffner, who decided that they should be given specific rank where there are more or less sharply defined differences in their antigenic structure, their epidemiological behaviour with respect to carrier-hosts, their behaviour in animals, their geographical distribution, and the clinical characters of the disease they produce in man. This view has practical advantages: different leptospiræ are carried by different rodents, and preventive measures must vary according to the host; and antiserum gives satisfactory therapeutic results only if it is specific for the infecting organism.

After describing techniques for demonstrating leptospiræ in blood and urine, he turns to serological methods. The agglutination-lysis test is the most generally useful, though it does not become positive until after the first week of illness, whereas leptospiræ can be seen in the blood in the first few days if differential centrifugalisation is used.

As leptospiræ can survive for short periods after ingestion by biting insects, mechanical transmission is a possible mode of infection; but in practice it is not an important one. The usual source of infection is contaminated water, and attention is therefore mainly directed to the means of contamination of water by vectors, to the conditions in which the leptospiræ remain viable and virulent, and to the most likely portals of entry in man when he is swimming, or working in wet rat-infested surroundings. The fouling of water may be prevented by destroying animal vectors, and proofing buildings, coalmines, and swimming-pools against them. Leptospiræ are destroyed by drainage of stagnant water or by increasing its acidity; in Japan calcium cyanamide was used successfully as a fertiliser in the rice-fields. Persons at risk can be protected with rubber boots and gloves, or immunised with killed vaccines or attenuated living cultures. To be effective, immunisation must be carried out with the species likely to cause infection; and difficulties arise in countries where there are several forms of leptospirosis.

Treatment, apart from the early exhibition of antiserum or penicillin, can proceed only on general lines. Neither arsenic, bismuth, or penicillin seems to affect the course of the severe infections once they are established. On the other hand, the benign leptospiroses are self-limited and specific therapy is unnecessary. On p. 110 experiments by Alston and Broom are quoted, showing that well-grown cultures of leptospiræ were not affected by high concentrations of penicillin. In those experiments, however, growth of young cultures was inhibited; so the results were not, as Professor van Thiel suggests, at variance with those of other workers who found leptospiræ susceptible to penicillin.

The second half deals individually with the 13 forms of leptospirosis separated on clinical, epidemiological, and serological grounds, and also with certain other less well-defined varieties. The epidemiology and the experimental findings in animals receive special attention, but the symptoms of infection in man are less fully presented. The book will be of value especially to epidemiologists and laboratory workers, and it should stimulate interest in a subject that has had relatively little attention here and in America.

Die Indikationen zur Röntgen- und Radium-Bestrahlung (Stuttgart: Thieme. 1948. Pp. 124).—Dr. R. Glauner, of Stuttgart, catalogues all manner of pathological conditions, discussing the extent to which treatment with X rays and radium is indicated. There is not much reference to world literature, and numerical proof is often missing. It is a little difficult to see for whom the book is intended, for it is hardly detailed enough for the specialist and might lead the practitioner to believe that radiation was a cure for almost any chronic disease; it does, however, serve as a reminder of the large number of conditions which may have a real interest to radiotherapists.

Fearless Childbirth (London: J. & A. Churchill. 1948. Pp. 99. 3s. 6d.).—Those who are interested in training women for childbirth should read this book. Miss Minnie Randell was one of the early workers in this field, and formerly principal of the school of physiotherapy in the department of physical medicine at St. Thomas's Hospital. She has devised a system of antenatal and postnatal exercises. Some of the diaries written by women about their labours are macabre and do not help to support the book's theme of safe, natural, and relatively painless childbirth.

Human Embryology and Morphology (6th ed. London: E. Arnold. 1948. Pp. 690. 40s.).—Sir Arthur Keith, F.R.S., maintains the evolutionary and comparative anatomical approach in the sixth edition of his well-known book on embryology. Two new chapters and many new figures and references have been added, and this stimulating and well-documented textbook now also reviews much of the new work done on embryology during the last 15 years. For the preclinical student there may be some lack of balance between function and the morphology; he may, for instance, be somewhat confused by the description of the cranial nerves in relation to "cranial segments" rather than to pharyngeal arches; but the book is in any case better suited to the more advanced student. Many B.N.A. terms are retained and a few of the text-figures are rather indistinct. These defects are not of great importance, however, in a book which in the past has aroused the interest of so many students in the subject of embryology, and which will undoubtedly be retained as an authoritative work.

Growth in Relation to Differentiation and Morphogenesis (Symposia of the Society for Experimental Biology, no. II. London: Cambridge University Press. 1948. Pp. 365. 35s.).—After a delay which we hope the editors and publishers will somehow contrive to reduce in future, the proceedings of the Society for Experimental Biology's symposium of July, 1947, were published last August in book form. The first volume was on nucleic acids; this second, edited by J. F. Danielli and R. Brown, is on various aspects of growth, and necessarily broader and vaguer in its outlines and much patchier in composition. Experimental embryology is in the doldrums just at present: in the last ten years little fundamental progress has been made in the theory of organisers, in spite of its promising beginnings, and the gap between embryology and genetics has yet to be closed by a structure stronger than is provided by after-dinner speculation. Nevertheless, there are rudiments here of work that will one day close that gap, and this volume will be of importance to those professionally interested in the problems of growth and differentiation. The medical man will find much in it to interest him, even if he cannot find room for it on his shelves.

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VARICOSE ULCER WITH ECZEMA
Healed beneath Pressure Bandaging

Fig. 1

CASE HISTORY

M.R. Aged 40. Housewife. Varicose ulcer with severe eczema right leg. (Fig. 1).

TREATMENT

August 9th, 1946.—Ulcer and surrounding skin cleaned with cod liver oil. Strips of Jelonet were applied to cover the ulcer and the eczematous area, with a pad of cotton-wool over the ulcer only. The whole leg was bandaged with Ichthopaste and then with Elastocrepe. (Fig. 2).

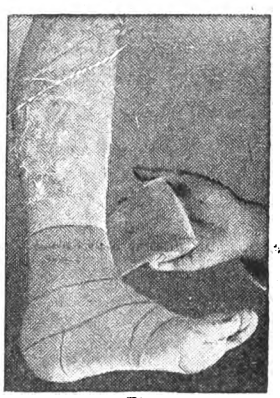

Fig. 2

August 23rd, 1946.—Ichthopaste and Elastocrepe bandaging repeated.

Sept. 13th, 1946.—The œdema was reduced and the leg much less painful. Calamine lotion was applied over the whole area with a pad of cotton-wool and felt over the ulcer, and the leg again bandaged with Elastocrepe.

October 4th, 1946.—Calamine lotion, pad of cotton-wool and Elastocrepe repeated.

October 11th, 1946.—Repeated.

November 1st, 1946.—Condition healed. (Fig. 3). The patient was instructed to continue application herself of calamine lotion and Elastocrepe.

COMMENT. In this case the eczema was more troublesome than the ulcer. Both responded to the soothing effect of Ichthopaste and the firm pressure of Elastocrepe. Details and illustrations above are of an actual case. T. J. Smith & Nephew, Ltd., Manufacturers of Jelonet, Ichthopaste and Elastocrepe are privileged to publish this instance, typical of many, in which their products have been used with success, in the belief that such authentic records will be of general interest.

Fig. 3

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The usual prognosis in Parkinson's Syndrome is such as to justify the introduction of any new remedy which shows definite promise, even in a minority of cases. Such a drug is

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THE LANCET

LONDON: SATURDAY, JAN. 8, 1949

Specialist Qualifications

WHAT makes a good "specialist"? Hardly the same things as make a great physician or surgeon or anatomist. Nobody would care to class OSLER or LISTER or JOHN HUNTER as specialists: their minds were too flexible, too full of expansive curiosities. Nevertheless, we should all like our specialists to share some of that greatness, that wide and questioning outlook; or at least we should like to be sure that their training will foster rather than impair such qualities. Nowadays those who wish to specialise, or (in the more pompous phrase) achieve consultant status in a specialty, are generally expected to take some higher examination. The patient, it is felt, must be protected from exploitation: if a doctor has passed the examination of a recognised authority he must know something about his specialty, and the public (and the profession) have a badge to go by. Undoubtedly this method of certification does much to restrict specialist practice to people with a background of relevant information; but at a time when new badges are being devised almost every day we shall do well to consider where all this is leading. May the higher examinations and diplomas do harm as well as good?

In the United States the certification of doctors as specialists is entrusted to some fifteen boards, each of which prescribes a course of training for its specialty and conducts examinations. At first sight this seems an admirable arrangement, setting a precedent that we might wisely follow. But in carrying the system to its logical conclusion our American colleagues have revealed its weaknesses as well as its strength, and we may usefully begin by noting what its critics say. Here, for instance, are some quotations from an address[1] by Dr. ALAN GREGG, director for medical services of the Rockefeller Foundation:

> The specialist groups began on the basis of respect for the self-imposed standards of excellence of their mutually chosen members. Did they realise what a profoundly different thing it was to change over to examinations as the basis of recognising excellence? . . .
>
> The chance of eventual recognition is a more encouraging circumstance for an original young specialist to deal with, than passing an examination set by those who can withhold approval of the new by insistent emphasis upon expert knowledge of the old. If the specialist groups had continued to elect their members on the basis of recognition of established competence, they would have avoided the serious danger they now run of being the unintentional partners of static and reactionary, albeit powerful and respectable, inertia or ignorance. . . .
>
> Are we prepared to believe that nipping the laggards is the essence of leadership, or that enforcing minimal standards will ever discover or encourage originality and advance? . . .
>
> If the greatest value for American medicine is to force up the general performance level of all specialists, by tending to the less fortunate, less trained, and less gifted, there is much to be said for certification boards. However, another way to raise the general performance level is to exert vigilant and jealous control in behalf of excellence, variety, and freedom to go beyond our present knowledge. The very years you pre-empt for the uniform training for the boards are the most precious in the lives of those young men from whom progress is to come. . . . The first ten years of an American doctor's professional life are apt to contain too many hours of waiting to use the skills and knowledge he has acquired. It is an inexcusable waste of the strength, the competence, and the ambition of thousands of young men, able and eager for a better use of their time. . . .
>
> There is some evidence that the press of candidates for certification has prevented some boards from considering what their long-term policies should be. The seriousness of the situation becomes more apparent when one realises that in some fields the numbers applying for certification are so large that the only way of reducing the examination to manageable proportions is by the true-false system of examination questions. Sometimes there is too little time to test the clinical competence of a candidate. The power the specialty boards possess is now increased to an uncontrollable degree because hospital boards and government services have discovered the comfort of passing the buck by letting certification be the basis of appointment, and in some cases of salary status.

We quote these remarks at length because some of them could be applied to the situation here as well as to the situation in the United States. The majority of the profession in both countries regard examinations for specialists as both necessary and natural: if (as everyone admits) prescribed courses and examinations are needed to enable the public to distinguish the qualified from the unqualified practitioner, what can be wrong with having further courses and examinations to ensure that the properly trained specialist is distinguishable from the pretender? Those who hold this opinion feel that the main object is to protect the public, by imposing tests that will exclude the incompetent. On the other hand there are experienced teachers and examiners who believe, with Dr. GREGG, that in setting up all this machinery for exclusion we are neglecting what really matters much more—the training of first-rate men. They would be content with a single qualifying examination for doctors, after which the future specialist, instead of spending his next few years under the shadow of a further examination in orthodox medicine, would at once begin to follow his own bent and would prove his worth by his work. According to this argument each new insistence on uniform experience and uniform knowledge is a fresh drag on original minds, and the whole approach is negative where it should be positive.

Examinations, with all their faults, have the merit of being relatively objective: their results do not depend on personal relationships and prejudices, and they seldom present any serious obstacle to men of first-class ability. Probably, however, most of us will agree that no examination can be sufficient in itself to decide whether a man should be recognised as a specialist. More important than the capacity to pass an examination is the capacity to do good work in the specialty; and recognition ought to depend largely

1. Delivered before the American College of Physicians at San Francisco on April 21, 1948.

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on the candidate having practised successfully at hospital over a considerable period. Some will go further and say that during this period the candidate's mind should be fixed on his work rather than on some academic ordeal to be faced at the end of it, and from this it would follow that any major examinations ought to be taken at an early stage of specialist training and should be conceived as a means of selecting those men and women suitable for training as specialists. Already it is customary at many hospitals to reserve the posts of registrar and chief assistant, and even others more junior, for holders of the M.R.C.P. and F.R.C.S.; which means that these qualifications, so far from conferring specialist status, are increasingly regarded as portals through which the young doctor must pass before he can gain his practical experience. In our last issue a correspondent writing on surgical examinations proposed that the Royal College of Surgeons should recognise the new state of affairs by a change of nomenclature that would transform its present members to licentiates and would make its membership examination a test of fitness for specialist training, which could be taken at any time after qualifying. The final examination, conferring the fellowship and specialist status, would not be undertaken until the candidate had had a thorough surgical training, and would be "much more difficult" than at present:

> To qualify for the fellowship the candidate should have received at least five years' practical surgical teaching from a recognised master, the first two years being devoted to general surgery and the last three, if desired, to some special branch of surgery. The examination should be a combination of general surgery and the specialty which the candidate chooses to offer: this latter part being conducted by specialists in that field. The candidate's standing with his master should be taken into consideration, and part of the examination should entail performing an operation in the chosen specialty at the hospital of an examiner, assisted by the examiner, and of conducting a ward round for the examiner.

As medical knowledge increases, the simplest solution to the problem of recognising specialists is to construct an ever more elaborate examination system. If this solution is rejected, and examinations are given a rather less dominant position in postgraduate education, we shall have to introduce alternative means of judging competence, but especially we shall have to get back to fundamentals and ensure that the future specialist has an adequate training. The dictionary meaning of the word "adequate" is not "some," or "moderate," but "enough"; and in this context it means enough to justify the profession and the public bestowing their trust. At the end of this training the would-be specialist must be able to satisfy some impartial adjudicating body that he has had sufficient experience to be called a specialist. But we shall create new dangers if the nature of this experience is defined too rigidly; for the rules must not be such as to exclude exceptional men who have left the beaten track. Here is a last quotation from Dr. GREGG:

> Freedom is more than a pleasure principle: it is a guarantee of vitality and survival through variety. Every tendency in our profession . . . that seeks to strengthen its position by means of standardisation, obligatory uniformity and unvarying acceptance deserves to be challenged as a threat to variety and survival.

Meat from Africa?

EVER since the repeal of the Corn Laws and the establishment of the principle of free trade, town-dwellers and business men in this country have given little thought to our sources of food. Since about 1890, except under the stimulus of war, neither the public nor the Government have taken much interest in home agriculture. They have often assumed that the English farmer is inefficient because his foreign competitor could produce food at a lower price; they have forgotten that this food was often produced on virgin land by methods which, as we now know, have ruined vast areas. During all this time the farmer and his men were commonly regarded as unintelligent yokels; it was not remembered that their forerunners, assisted by the great pioneer landlords, had developed one of the most efficient methods of farming in the world and evolved nearly all the outstanding breeds of livestock—breeds which have been exported to distant lands and now provide us with our imported meat, wool, and dairy products. Similarly, little attention was paid in Great Britain to agricultural or veterinary research. Fortunately, however, a more enlightened policy was followed in the Commonwealth. It was largely through THEILER'S [1] brilliant and versatile researches that livestock farming in South Africa became possible; and it is in Africa more even than other continents that further agricultural development depends on scientific discovery and its application. For example, cattle plague (rinderpest) killed a large proportion of African cattle during the 1890s, and widespread use of modified virus vaccine, devised in India by J. T. EDWARDS,[2] is still required to keep this disease under control. The other major menace to African livestock is trypanosomiasis, which prevents stock-raising over $4^1/_2$ million square miles; and there is a danger that its vector, the tsetse fly, will spread further.

Some four years ago, when the work leading to the production of proguanil ('Paludrine') at the Imperial Chemical Industries laboratories in Manchester had been largely completed, attention turned to the chemotherapy of trypanosomiasis, in which the results obtained with the compounds at present in use fall far short of the ideal.[3] The team was led on the chemical side by Mr. F. H. S. CURD, PH.D. (who was killed so tragically in a train accident last month), and on the biological side by Mr. D. G. DAVEY, PH.D., both of whom played a large part in the discovery of proguanil. Of many substances tested, the compound '7555' gave the most promising results, in mice, against *T. congolense* infection, which is probably the most difficult to treat. Pharmacological studies were then carried out in calves, but the Chief Veterinary Officer did not think it safe to study this infection in cattle in Great Britain, and arrangements were made with the Colonial Office for Dr. DAVEY and Mr. J. S. STEWARD to carry out experiments in infected areas of Africa. They had the active help of the veterinary departments in the various territories, including the Sudan, and the results of their work, announced last week by the Colonial Office in con-

1. Theiler of Onderstepoort. British Commonwealth Leaflets, series A, no. 4. H.M. Stationery Office. 1948.
2. See *Vet. Rec.* 1946, 58, 501; *Ibid*, 1948, 60, 361.
3. Wilson, S. G. *J. comp. Path.* 1948, 58, 94.

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junction with Imperial Chemical Industries, suggest that 'Antrycide' (as 7555 is now called) will cure all forms of trypanosomiasis in cattle, horses, camels, and other animals. Trials in East Africa and the Sudan showed that a single treatment would cure cattle of *T. congolense* and *T. vivax*, the two worst forms of the disease; it was also used with success against *T. brucei* infection in cattle, horses, and dogs, against *T. evansi* in cattle, and against *T. simiæ* in pigs. The outstanding property of the drug, however, is its apparent ability to prevent infection for up to six months, presumably because a deposit at the site of inoculation produces a persistent blood-level.

When Mr. D. R. REES-WILLIAMS, under-secretary of State for the Colonies, described antrycide as "one of the great advances made in science" he was perhaps confusing a discovery of practical importance with one of intrinsic value to science itself. CURD, DAVEY, and their colleagues deserve great credit for this work, which has brought them a second practical success so soon after the first; but even if the new drug fulfils all the high hopes now aroused it will not necessarily solve all the problems associated with the tsetse fly. It is well to recall SWYNNERTON'S conclusion [4] that even if an effective method of immunisation were found—and chemoprophylaxis by the drug is similar to immunisation—this would not constitute a complete solution. Experience of tsetse flies and trypanosomiasis induces a certain caution before claiming a victory.[5] There may yet be many difficulties: for example, though it is true that the drug can be injected by uneducated African natives, a great deal of supervision is required in all large undertakings of this sort, and the veterinary departments are still woefully small in relation to the vast areas involved. The tsetse fly has sometimes proved surprisingly susceptible to slight ecological changes, and the settlement rendered possible by this drug may, if properly planned, cause the fly to disappear from large areas. I.C.I. are hoping to produce 2–3 tons of antrycide this year—already enough to treat about 2 million animals. But even if, as we all hope, the drug, under varied conditions, fulfils its early promise, it will clearly be four or five years before it can have any great influence on meat production. In any event, because of changed economic conditions and the troubled state of the world, the people of this country should not be led to expect large supplies of cheap food from abroad, but should be continually reminded that the best and safest source of good food is our own countryside. Happily there is some indication that this lesson is being slowly learnt.

SWYNNERTON took the rather surprising view that in the past the tsetse has done an invaluable service in saving great areas from becoming peopled, exhausted, and ruined. Describing the various types of flora which can be produced by man's intervention he wrote:

> "Our third picture—that of the future—should be one of pleasant cottages with fruit trees, shady groves of the native trees preserved tsetse-less and other trees planted, rotation of crops in well-manured fields, a regulated number of cattle to the square mile, grass close-grazed and improved but not destroyed, and, in places, large nature sanctuaries, judiciously chosen and 'managed' (in the technical sense) for the perpetuation of the old flora and fauna and used not merely for this but for the delectation of the people, white and black.
>
> "But, in reclaiming new country, we must plan for all this from the start. It will be too late when the land is destroyed as the result of hand-to-mouth settlement methods: I do not believe that we have in the past shown fully our fitness to reclaim; but I do think I see the cloud, as yet no bigger than a man's hand, that indicates that the pleas of the apostles of anti-erosion are at last producing an impression, and that the land we reclaim in the future will be subject to regulated settlement and limitation of the numbers of its cattle.
>
> "If I am right, we are justified in continuing to reclaim—for the relief of existent erosion and the fuller development of the country." [6]

It is to be hoped that the Colonial Office announcement implies a determination to live up to SWYNNERTON'S ideals.

Histoplasmosis and Torulosis

THE systemic infections by moulds still rank among the rarities of medicine—the only systemic mycosis with which most doctors in this country are familiar is actinomycosis—though the dermatophytoses (ringworms) are common enough. However, increasing knowledge of the epidemiology and pathology of this group of diseases, and especially the development of tests which will reveal latent or minimal infections, is showing that some of them are widespread. The histoplasmin test, based on the same principle as the tuberculin test, is not yet completely specific, but the discovery that in the central eastern U.S.A. many children with X-ray appearances suggestive of pulmonary tuberculosis were tuberculin-negative but histoplasmin-positive led to intensive clinical and mycological studies which have brought to light unsuspected cases of active histoplasmosis.[7] Officers of the U.S. Public Health Service, in a study of student nurses which has included 23,000 since it began in 1943, have established interesting though not conclusive correlations between pulmonary infiltrations and histoplasmin sensitivity.[8] There seems to be a definite association between nodular infiltrations, widely distributed throughout the lungs, and positive reactions to the histoplasmin test.

The first three reported cases of histoplasmosis, all fatal, were described by DARLING [9] in Panama in 1906. He considered the organism, *Histoplasma capsulatum*, to be a protozoon, but ROCHA-LIMA [10] and DE MONBREUN [11] established its fungal nature. The yeast-like fungus can easily be cultivated on Sabouraud's medium. Like other fungi causing systemic infections it is dimorphic, with saprophytic and parasitic forms. Nothing is known about its natural saprophytic life, but in cultures it produces mycelia and spores, whereas in the tissues it usually appears as a round or oval gram-positive cell, 3–5 μ in diameter, consisting of a round or crescentic

4. Swynnerton, C. F. M. *Trans. R. ent. Soc. Lond.* 1936, 84, 1.
5. *Lancet*, 1948, i, 951; *Ibid*, ii, 819.
6. Loc. cit. (ref. 4) p. 465
7. See Duncan, J. T. *Trans. R. Soc. trop. med. Hyg.* 1948, 42, 207.
8. Edwards, L. B., Lewis, I., Palmer, C. E. *Publ. Hlth Rep., Wash.* 1948, 63, 1569.
9. Darling, S. T. *J. Amer. med. Ass.* 1906, 46, 1283.
10. See Iams, A. M., Tenen, M. M., Flanagan, H. F. *Amer. J. Dis. Child.* 1945, 70, 229.
11. de Monbreun, W. A. *Amer. J. trop. med.* 1934, 14, 93.

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central mass surrounded by a clear zone and a refractile capsule. It is pathogenic for monkeys, young dogs or mice, guineapigs, and rabbits. Up to 1947, there had been 88 human cases on record,[12] about a quarter of them being in children; the youngest victim was only 7 weeks old, but there is no evidence that the infection is acquired in utero. Most cases have been reported from the U.S.A., and the Mississippi basin has accounted for more than any other area, but single cases have been identified in many parts of the world. The pathological changes are of two types. Nodules with a necrotic centre may be found, surrounded by fibroblasts, new capillaries, lymphocytes, and large mononuclear cells which often contain the organisms. With or without these focal lesions there is a widespread hyperplasia of reticulo-endothelial cells, which may contain large numbers of encapsulated organisms; the ileum and colon may show ulcerative lesions. In infants histoplasmosis is characterised by fever, anæmia often with leucopenia, enlargement of liver and spleen, and commonly gastroenteritis and respiratory symptoms. It may be confused with Hodgkin's disease, leukæmias, tuberculosis, cystic disease of the pancreas, hæmolytic disease of the newborn, or congenital syphilis.[12] In older children it is mainly a pulmonary disease, often resembling tuberculosis and often symptomless. In adults it may be a localised nodular and ulcerative affection of the skin and/or mucous membranes or a generalised disease involving the lungs, gastro-intestinal tract, joints, and heart. Histoplasma may be found in the blood by the "thick drop" method or by cultures, but bone-marrow biopsy seems to be the most reliable method. The organisms may be present not only in monocytes but also in megakaryocytes and neutrophil and eosinophil leucocytes. There seems likely, before long, to be a reliable skin, complement-fixation, or precipitin [13] test.

In this issue Dr. DANIEL and his colleagues at the Radcliffe Infirmary describe two examples of systemic infection with another yeast, *Torula histolytica* or *Cryptococcus hominis*, which has a particular affinity for the central nervous system. The organism is sometimes called blastomycoides, and cases of this disease have been reported as blastomycosis, but it should not be confused with Gilchrist's disease due to *Blastomyces dermatitidis*. Torula causes a chronic meningitis or meningo-encephalitis, but a generalised infection has been described.[14] The most conspicuous clinical finding, especially in children, is an extreme opisthotonos. There is emaciation, mental deterioration, and sometimes blindness. The cerebrospinal fluid shows an increase of globulin and a high cell-count. Yeasts are often present in the fluid, and in routine examinations are commonly confused with lymphocytes. At necropsy a gelatinous exudate, not unlike that in tuberculous meningitis, is found in the great cisterns at the base of the brain. The leptomeninges all over the base and vertex may be studded with pin-head greyish nodules which are submiliary granulomata consisting mainly of large mononuclear cells. In some granulomatous lesions there are giant cells of the Langhans type and many lymphocytes. Necrosis is not common in the small meningeal granulomata. Organisms are usually abundant but occasionally very scanty. The disease may be limited to the meninges or may be associated with small necrotic foci or cysts with a gelatinous material in the cortex, and a cyst as big as a hen's egg has been described.[15] According to CHIARI,[14] necrotising foci with nonspecific inflammatory changes and miliary abscesses represent early lesions. The yeast cells are spherical, 14–18 μ in diameter, surrounded by a clear halo which is best seen in indian-ink preparations. Cell plus clear zone measures 25–40 μ across. Budding, but no mycelia, is usually seen in tissues and cultures. The organism is pathogenic for mice and guineapigs, but rabbits appear to be immune. It has been found in milk, in transfusion plasma, on preserved fruits and other food, and on the human skin and mucosæ. The organism may gain entry to the blood-stream through the nasopharynx and tonsils, but DUNCAN [7] suggests that the principal mode of infection is by the inhalation of the dry yeasts.

12. Iams, A. M., Keith, H. M. *J. Pediat.* 1947, **30**, 123.
13. Pates, A. L. *Science*, 1948, **108**, 383.
14. Chiari, H. *Wien. klin. Wschr.* 1931, no. 43. Reilly, E. B., Artman, E. L. *Arch. intern. med.* 1948, **81**, 1.
15. Gray, F. C. *S. Afr. med. J.* 1940, **14**, 65.
16. Given at the Royal College of Physicians on Dec. 7 and 9, 1948.

Annotations

PLAGUES AND THE FORTUNES OF MEN

WARS and pestilence have brought down many lofty civilisations. Troubled for our own, and made fearful by experience, we may be pardoned for looking most anxiously at the first of these two causes of decline; but study of the evidence suggests that pestilence has been even more destructive than war. Occasionally, as Prof. W. H. Wynn pointed out in his FitzPatrick lectures,[16] it has operated to man's advantage, and has preserved a valuable civilisation by destroying its oppressors. Perhaps the most striking example is that of the epidemic of bubonic plague which struck the Philistines after they had captured the Ark of the Covenant. They died by thousands; and but for that slaughter this formidable people might well have wiped out the Israelites, and with them our hope of Christian culture.

The earliest recorded epidemic befell the Hittites, a flourishing civilisation in Mesopotamia from about 1750 B.C. onwards, though their culture went back much earlier than that. Cuneiform records on clay tablets found in Asia Minor tell how the son of the Hittite king set out to marry a widowed Queen of Egypt, but died soon after his arrival in her country. His angry father declared war on Egypt and invaded Syria; he won several victories, but sickness broke out among his soldiers and spread to the civil population on their return home. The disease (probably smallpox) remained endemic for twenty years, and killed many—among them the king and his son who succeeded him. The Hittites were weakened so much that their subject tribes revolted, their army was crippled in the Egyptian war, and finally the Achæans, after taking Troy, drove them into Syria where the Assyrians overwhelmed them. Their empire of a thousand years melted away leaving hardly a trace—heavy work for a virus. At the siege of Troy an epidemic—probably of glanders—among the Greek mules and dogs spread to the besiegers, and nearly turned the scale for the Trojans. The first Persian invasion of Europe, by Darius, was checked by a dysentery epidemic among the Persian troops; and in the second invasion they suffered their famous defeat at Marathon, when the small body of 9000 Athenians

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charged down from the hills on the 40,000 Persians and drove them into the sea. At the third invasion, under Darius's son Xerxes, the Persian troops were crippled in a sea fight and had to retreat on foot. Starving and thirsty, they ate grass and drank polluted water; thousands died of dysentery, and as a result of this epidemic Persian aggression in Europe was finally destroyed.

Many other famous epidemics have changed the course of history: for example, the destructive outbreak of smallpox which heralded the decline of Athens; the malaria brought back by the ill-fated expedition against Egypt, to remain indigenous in the regions round Athens to this day; the plague which forced the Gauls to retreat from Rome, leaving the Capitol still untaken; the infections (possibly malaria and dysentery) which undermined Hannibal's invading Carthaginians; and the pestilence (smallpox again) which killed Marcus Aurelius in Vienna, and so wasted the power of Rome that it became prey to the barbarians. Professor Wynn, who plans to follow this fascinating study down to modern times, suggested that though the primary cause of the fall of civilisations must be sought in the minds and hearts of men, yet bacteria and viruses are still man's greatest foes, and civilisation is constantly threatened by them as well as by war. If today our minds and hearts are as bad as ever, at least our epidemiology and hygiene are much better: we may survive, and even repent.

AUREOMYCIN: A VERSATILE ANTIBIOTIC

AUREOMYCIN, a new antibiotic which can be given by mouth,[1] is active against many of the rickettsiæ, certain viruses, and many gram-negative and gram-positive organisms. Preliminary reports indicate that among rickettsial diseases in which it is effective are Rocky Mountain spotted fever, Q fever, typhus, and rickettsial pox (a relatively new disease of which there has lately been an outbreak in New York). Experimental work has shown that it is potent against the psittacosis virus; and some cases of primary atypical pneumonia seem to have responded very favourably to its administration. There is reason to hope that in brucellosis the results with aureomycin will be better than with any previous treatment. Infections with the coli-aerogenes group, particularly those affecting the urinary tract and peritoneum, have been successfully treated with it; and it is now being tested with salmonella infections, including typhoid fever.[2] Moreover, since it readily passes the blood-brain barrier it may prove useful in some forms of meningitis. It is active against many of the organisms not affected by penicillin or streptomycin. According to Finland et al.,[2] most organisms do not become resistant to it as they do to streptomycin; and there is already evidence of its usefulness against gram-positive organisms that have become penicillin-resistant.

In screening experiments aureomycin was found to be highly effective in the treatment of mice infected intracerebrally with the virus of lymphogranuloma venereum. Impressed by these preliminary tests, Wright and his colleagues,[3] at the Harlem Hospital, New York, used this substance to treat 25 patients suffering from the disease. The cases were divided into three groups—buboes, lymphogranulomatous proctitis (with or without ulceration), and benign cicatricial rectal structures. All of 8 patients with buboes showed a decided reduction in the size of the glands after four days' treatment; within forty-eight hours, only occasional elementary and inclusion bodies were seen in the buboes, and after a week's treatment none at all were observed. Of 3 cases of proctitis each was considerably improved, tenderness and discharge disappearing within four days and bleeding in eight. Finally, in 14 patients with benign rectal stricture there was a decrease in rectal pain and in discharge and bleeding, and an increase in the stool diameter. These results are encouraging in a disease for which there has hitherto been no specific treatment. Wright and his associates noted mild hypochromic anæmia in all who received aureomycin parenterally. This was not severe enough for treatment to be stopped, and it responded to treatment with folic acid and iron; subsequently the anæmia was shown to be largely due to the solvent used for the aureomycin.

This antibiotic also seems to be effective in a number of ocular infections. Braley and Sanders,[4] of Columbia University, have used it locally as a 0·5% solution of a borate salt, in saline. Milder infections such as inclusion conjunctivitis, vernal, follicular, and influenzal conjunctivitis, and conjunctivitis due to staphylococci and pneumococci improved within a matter of hours and cleared in one to two days. Epidemic keratoconjunctivitis and dendritic keratitis were more resistant, requiring protracted local and parenteral treatment. In epidemic keratoconjunctivitis aureomycin was of value only when treatment was started before the fourth day of the disease; with dendritic keratitis and Mooren's ulcer results were equivocal. No patients with trachoma were treated, but it is thought that aureomycin should be useful in this condition. In the opinion of Braley and Sanders it is at least as effective as penicillin when applied locally, and it is non-irritating to the inflamed eye.

Unlike streptomycin aureomycin is virtually non-toxic in therapeutic doses; the only side-effects so far observed are occasional nausea and some pain on injection, which will no doubt disappear with the elimination of impurities. It will almost certainly earn a place alongside penicillin and streptomycin.

NEW YEAR HONOURS

IT seems only yesterday that Sir John Boyd Orr, of the Rowett Institute, was speaking his persuasive words in *World of Plenty*. But the intervening years have given him vast new audiences who have understood for the first time the practical importance of the science of nutrition, both for themselves and for the nations. His earnestness and his exposition have released a great constructive force that will go on acting whatever he himself may now do; but it is entirely right that he should have the permanent place among our legislators which a peerage now gives him. Another man who, in his own less conspicuous way, has done a great deal to apply scientific knowledge to everyday life is Sir Wilson Jameson, now appointed G.B.E. Medicine is fortunate both in the wisdom and in the loyalty of its senior representative in the Civil Service during a decade of unparalleled difficulty, and fuller knowledge of his service will deepen the respect in which he is held on all sides. Sir William Gilliatt's K.C.V.O., though it commemorates a happy event, has been earned in many years of valuable work. Of the new knights, Prof. Henry Cohen is well known as a clinician and as the principal author of the B.M.A.'s report last year on medical education; and he has lately assumed a major professional responsibility as vice-chairman of the Central Health Services Council. He combines common sense with uncommon distinction of mind. Mr. H. E. Griffiths, who also receives a knighthood, is a surgeon whose original interest in industrial injuries has widened into long and devoted advocacy of better reablement. Prof. Sydney

1. Annotation, *Lancet*, 1948, ii, 618.
2. Finland, M., Collins, H. S., Paine, T. F. jun. *J. Amer. med. Ass.* 1948. 138, 946.
3. Wright, L. T., Sanders, M., Logan, M. A., Prigot, A., Hill, L. M. *Ibid.* p. 408.
4. Braley, A. E., Sanders, M. *Ibid*, p. 426.

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Smith, third of the medical knights, is an adopted but cherished son of Edinburgh who has won enviable reputations as professor of forensic medicine, as dean of the medical school, as acting principal of the university, and as much besides. The many other honours which we are glad to record on p. 77 include a Privy Counsellorship for Dr. Edith Summerskill, in recognition of her expertness as a parliamentarian.

A LITTLE NURSING?

Two students write today to protest against the introduction of three weeks' nursing experience into the medical curriculum as "a ridiculous waste of time." They hope this innovation will not spread to other hospitals, and plead instead for "at least one forceps delivery." Our sympathies are often with students when they criticise the curriculum, but we cannot share this view, which seems to reflect a regrettable bias given to the doctor's professional outlook by current training. Mr. Carruthers and Mr. Richardson feel that the student, by watching the nurses at work in the wards, can acquire a technique which he should later constantly use and teach to others—that of making people comfortable. It cannot be acquired by observation alone, or, for that matter, by three weeks' instruction: good nursing comes with practice. But though three weeks will not make the student a good nurse it will at least teach him the rudiments and some of the difficulties of an important side of his job. Other hospitals would do well to follow the London Hospital's lead.

DOES SODIUM SALICYLATE CURE RHEUMATIC FEVER?

UNDER this title Reid [1] has published an article in which he postulates that "adequate oral administration of sodium salicylate can really cure the disease"—rheumatic fever. This assertion is based on observation of 9 adults, and of 3 children with pericarditis. Of the adults 7 were given sodium salicylate 2 g. and sodium bicarbonate 2 g. at four-hourly intervals from 6 A.M. to 10 P.M.—five doses daily—until "complete recovery as indicated by the return of the erythrocyte-sedimentation rate to normal." The other 2 adults received the same amount of sodium salicylate but no alkali. To 2 of the 3 children (aged 14, 12, and 9 years) sodium salicylate 1·3 g. and sodium bicarbonate 1·3 g. were given at the same intervals as for the adults; the third child received this dosage of sodium salicylate but no alkali. Reid gives evidence that the efficacy of salicylate treatment depends upon the attainment and maintenance of a plasma-salicylate level of 30–40 mg. per 100 ml.; he also suggests that the urinary concentration of salicylate is a satisfactory guide to the plasma concentration. He found the fall in the sedimentation-rate to be closely correlated with the plasma concentration of salicylate; failure to respond to salicylates is attributed by him to neglect to maintain a satisfactory plasma-salicylate level and to withdrawal of salicylates at too early a stage. "The practice of giving large doses of salicylate until fever, tachycardia, and joint pains have been relieved and then drastically reducing the dose is condemned."

This is a valuable contribution to an ever-vital problem. But the series is small; and it is perhaps risky to base conclusions upon a study principally of adults, for a first attack of rheumatic fever after the age of 20 seldom causes permanent damage to the heart. (This criticism can also be levelled against some American reports, such as those of Coburn [2] and Manchester,[3] in which a curative action is claimed for salicylates.) The third criticism is that no mention is made of any follow-up. The criterion of cure in this series—the sedimentation-rate—was also used by Coburn. Yet there is still no good evidence that the effect of salicylates in lowering the sedimentation-rate implies a parallel beneficial action on the rheumatic process. Rapoport and Guest [4] found in 15 patients with a raised sedimentation-rate, of whom only 4 had rheumatic fever, that the administration of salicylate caused a fall in the sedimentation-rate; and Homburger [5] reported a similar finding in patients with carcinomatosis. The most relevant contribution, however, is that of Harris.[6] Using full doses of salicylate (at least 1 grain per pound body-weight) he found that, of 6 patients with pulmonary tuberculosis and 4 with rheumatoid arthritis, 8 showed a fall in the sedimentation-rate of the order observed in patients with rheumatic fever under such treatment. In a further series of 5 children with rheumatic fever, chosen because (*a*) they had leucocytosis, (*b*) the white-cell count was not affected by salicylate, and (*c*) there were no manifestations of salicylate toxicity, he found that although the sedimentation-rate fell to normal the white-cell count still reflected continuing activity and there was no definite indication of clinical improvement. Cautiously Harris concludes: "It is very doubtful that massive salicylate therapy suppresses the inflammatory reaction of the rheumatic patient or that the lowering of the E.S.R. in rheumatic patients so treated has the significance attributed to it by Coburn."

The history of salicylates in the treatment of rheumatic fever since they were first introduced for this purpose by Maclagan in 1876, does not suggest that they cure this disease. They have been used so widely and for so long that it is hard to believe that if they had a curative action this would not have been recognised long ago. There certainly would not have been reports, such as those of Miller,[7] Ehrstrom and Wahlberg,[8] and Master and Romanoff,[9] suggesting that the outcome of rheumatic fever in children is alike whether or not salicylates are given. Ehrstrom and Wahlberg's conclusions were based upon a series of 51,111 cases, while Miller's were based upon 1907 patients treated with salicylates and 1600 who received no salicylates. Even the argument that the earlier workers did not use large enough doses is not valid; as long ago as 1903 Lees [10] suggested doses up to gr. 300 daily, while in 1906 Clarke [11] was giving gr. 240 daily. Recent work indicates that this is more than enough to maintain the optimum plasma-salicylate level. Maggioni [12] has shown that in children the optimum level can be maintained with a dose of gr. 1–1·5 per pound body-weight (0·12–0·18 g. per kg.).

THE KING'S HEALTH

LAST Monday the following bulletin was issued from Buckingham Palace:

Since the bulletin of Dec. 13, 1948, the King has made uninterrupted progress. His general health is entirely satisfactory. On both right and left sides the arterial circulation in the legs and feet is improving slowly. It is not yet sufficient to allow more than strictly limited activity when His Majesty leaves London to continue his convalescence in the country.

MAURICE CASSIDY
THOMAS DUNHILL
HORACE EVANS
J. R. LEARMONTH
J. PATERSON ROSS
MORTON SMART
JOHN WEIR.

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Special Articles

THE NATURAL HISTORY OF THE COMMON COLD

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From the Common Cold Research Unit, Harvard Hospital, Salisbury, Wilts *

ATTEMPTS to prevent or cure colds are held up by ignorance of what may be termed the natural history of the disease. On the one hand, it is often evident that a cold is "caught" by contact with one who is already a victim. On the other hand, colds often appear to be acquired quite otherwise—e.g., through getting the feet or body wet or chilled. Some observers deny the truth of this last view of the causation of colds and think infection all-important. Others go to the opposite extreme and deny that cross-infection plays any part at all. In this difficult field accurate observation and experiment are both of value, and an attempt will be made to see how far each method can contribute to a solution of the problem. At present the gaps in our knowledge are very great. We should, for instance, dearly like to know the answers to the following eight questions or groups of questions:

(1) Is the common cold an entity or a group of diseases? If it is an entity, how variable is its clinical course?
(2) What is the causal agent—bacterium or virus or neither? What are its properties?
(3) How long can the agent persist (*a*) in the host, (*b*) outside?
(4) Is infection always caught from another victim? Or can it be activated in a subject already harbouring the agent?
(5) If it is "caught," what are the means of spread?
(6) If it is activated, what stimuli are effective and through what mechanism?
(7) What explains the seasonal incidence?
(8) Why does resistance vary from one person to another and in one person from one year to another?

Though none of these questions can be fully answered, pertinent information is available from several sources. Observation of happenings in semi-isolated communities has provided some of this. A clear answer to the first three questions could probably be obtained readily enough if we had a convenient susceptible laboratory animal or any of the numerous techniques now available for the study of influenza virus.

The Common Cold Research Unit in Salisbury set up by the Medical Research Council and Ministry of Health in 1946, had as its primary objective the discovery of a laboratory technique with which colds could be conveniently studied. It was obvious to those concerned that without such a technique progress must needs be very slow. At the beginning the work had necessarily to be based on the testing of materials on human volunteers as the only technique available. During the two and a half years of the unit's existence some knowledge about colds has been acquired—in part as a by-product of the main endeavour—and this bears on several of our eight questions. Before dealing with these in turn, an account will be given of the conditions of study at the Salisbury unit. These have been briefly described before (*British Medical Journal* 1947, Andrewes 1948).

THE COMMON COLD RESEARCH UNIT

A unit for research into the common cold was established at Harvard Hospital, Salisbury, in the summer of 1946 as a joint project by the Medical Research Council and the Ministry of Health. The name "Harvard" commemorates the part played by Harvard University in establishing and staffing this hospital unit in Salisbury in 1940–41. At the end of the 1939–45 war it was handed over by American generosity to the Ministry of Health; its earlier history has been described (*British Medical Journal* 1947). It consists of the twenty-two prefabricated huts sent over from America and some Nissen huts and other outlying buildings added later. Six of the main huts have been divided into two, to provide twelve "flats" for human volunteers; these are connected by covered runways. Others of the huts are used as laboratories, staff quarters, &c. Each of the volunteers' flats is planned to accommodate two people; we thought that few would relish the prospect of ten days' solitary confinement.

THE VOLUNTEERS

We have used our volunteers almost wholly as indicators of the presence of a cold-producing agent in test materials. For instance, after attempted cultivation of a virus in eggs, material from the egg is tested on volunteers to see whether the virus has survived. Each member of a pair of volunteers always receives an inoculum of the same material. We at first recruited almost all our volunteers from among university students during their vacations, but later obtained many from industrial firms, especially Messrs. W. D. & H. O. Wills, from the British Red Cross, and by appeals to the general public through the help of the press and the B.B.C. People between the ages of 18 and 40 were asked to come forward; they had to be free from a history of tuberculosis, asthma, hay-fever, and recurrent sinusitis. In two and a half years we have had 899 visits from volunteers; this figure does not involve 899 separate persons, for many have been two or three times. Return visits are allowed after six months' interval.

AMENITIES AND PRECAUTIONS

To evoke a regular flow of volunteers, conditions are made as attractive as possible. Railway fares to and from Salisbury are paid, and volunteers receive 3*s*. a day pocket money. Each "flat" for two persons contains a sitting-room, a dining-room, two bedrooms, a medical room, a bathroom, and a W.C. Sitting-rooms are provided with a wireless set and a telephone. Indoor games and books are provided, and there are facilities, in outlying huts, for playing table-tennis and other games between partners. Precautions are taken to obviate the risk of cross-infection when one recreation room is used later by another pair. Country walks are allowed on condition that built-up areas, buildings, and vehicles are avoided; and volunteers are asked to keep 30 ft. away from people they meet. Their only human contacts during this ten-day isolation are with their own partners and with the masked and gowned doctor and matron who visit them daily. Individual thermometers and other medical equipment are provided, and each hut has its own crockery, cutlery, and vacuum containers for the delivery of hot meals. These hot meals are left at the entrance to the flats three times a day. Between each ten-day trial a four-day period is used for cleaning out the flats and their contents. No precautions are taken to prevent possible introduction of infection on papers, letters, or the outside of food containers, milk bottles, &c.; nor are books, games, and furniture sterilised between trials.

ROUTINE OF TRIALS

Volunteers arrive on a Wednesday morning, are met at Salisbury station, are brought to the hospital, and have a talk explaining the nature of the trial and the

* The work from Harvard Hospital is presented on behalf of the Common Cold Research team. Many of the ideas put forward in this paper arose in course of discussion within the team. Members of the team: (*a*) those engaged wholly or mainly on this problem, C. H. ANDREWES, M.D., F.R.S., the late D. K. M. CHALMERS, M.D., D.P.H., K. R. DUMBELL, M.D., F. FULTON, D.M., E. J. LOWBURY, M.B., T. SOMMERVILLE, M.B.; (*b*) others collaborating, W. H. BRADLEY, M.D., J. A. DUDGEON, M.D., W. J. ELFORD, D.SC., D. HORSTMANN, M.D., J. S. F. NIVEN, M.D.

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reasons for the rules necessary to avoid accidental infection; they then disperse to their flats. They have a routine clinical and X-ray (chest and sinuses) examination and are then observed for three days in case any should already be incubating a cold. All who are not free from signs and symptoms are, together with their partners, excluded from the main trial, but most of these can be used in other studies. On the Saturday they are inoculated intranasally, 0·5 ml. of fluid being run into each nostril with the patient supine. This position is maintained for 2 min., and the person is instructed not to blow his nose for half an hour. A similar technique is used when it is desired to wash out a person's nose to obtain a fresh supply of infectious material. About 10 ml. of saline solution is run into the nostrils a little at a time and then caught in a petri dish when the person tilts his head forward.

Sheets for daily recording of symptoms by the volunteers are provided; the matron visits each flat daily and records temperatures and pulse-rates, and immediately afterwards the clinician makes his round. He notes such signs as watering of the eyes, evidence of nasal obstruction and discharge, and any abnormal signs in nose or throat. He inquires about the amount of nasal discharge during the day, sore-throat, cough, and other symptoms. In practice most information is obtained by inspection of the handkerchiefs used during the past twenty-four hours and of the secretion expelled "on demand." Gross changes in nose and throat have almost always been associated with definite subjective symptoms. An attempt has been made to gauge the severity of colds by giving "marks" for each sign or symptom, greater weight being placed on the objective signs. Colds are finally assessed as severe, moderate, mild, doubtful mild, or absent. For purpose of analysis the "doubtful mild" colds are classed as negative.

PRECAUTIONS AGAINST SUBJECTIVE ERRORS

Frank colds are readily diagnosed. Our test materials, however, often produced symptoms which in the aggregate were significant but which in any one case were hard to interpret. We guarded as carefully as we could against bias, on the part both of volunteers and of observers, which might affect accurate interpretation. Most trials included instillation into some subjects of "control" supposedly inert material. Before inoculation, control and test materials were distributed into bottles, each containing enough for two people and labelled with a different letter. With a table of random numbers the bacteriologist, who alone knew what each bottle contained, allotted one lettered bottle to each flat. Thus volunteers did not know what they were getting nor whether we were expecting them to catch a cold or not. The clinical observer did not know what any pair received until he had committeed himself in writing at the end of the trial as to which had developed a cold and which had not. Even if three pairs had received the same inoculum, these would have been given material from bottles labelled with three different letters; so the clinician would have found it a difficult feat, even if he had tried to guess. From knowledge of their own intense interest in the results of tests, all members of the team felt that this enforcement of complete objectivity was of first-class importance.

This "control" system had the advantages of assuring us, as the study proceeded, that our preliminary quarantine period was long enough and that our isolation precautions were adequate. In practice, of 47 volunteers receiving sterile serum-broth intranasally, 2 developed doubtful mild colds and 45 remained symptom-free. We can now consider how far our studies and those of other workers can give answers to the 8 questions propounded above.

IS THE COMMON COLD AN ENTITY?

One can be fairly sure that several infections induce symptoms such as most people call "colds." We, like several other observers, have produced mild symptoms of a cold by inoculating influenza-A virus attenuated for man by long-continued cultivation in fertile eggs; such symptoms were induced in our trials in 3 of 15 inoculated subjects. It is likely that, in normal circumstances, influenza virus can produce mild cold-like symptoms in some relatively immune people. Dingle and his co-workers (Commission on Acute Respiratory Diseases 1946) have reported that an agent producing atypical pneumonia in some people gave rise in others to symptoms of a common cold; in both groups the incubation period was to 14 days. On the other hand, we have stored at −76°C two strains of cold-producing agents for many months, and with these and materials obtained by serial passage of them through man have produced a disease with only a moderate range of variation in signs and symptoms. Some roughness or soreness of the throat developed in 61 of 88 of these experimental colds, usually right at the onset. The incubation period was normally 2 or 3 days (see table I) with a range of 1–6

TABLE I—INCUBATION PERIODS OF EXPERIMENTAL COLDS

Length of incubation (days)	1	2	3	4	5	6
No. of definite colds	9	37	34	7	3	2
No. of doubtful mild colds	0	6	5	1	6	1

days. Nasal discharge was an almost invariable symptom; it was usually thin and serous at first but sometimes viscid from the beginning. Twenty-four hours after the onset it was commonly mucopurulent. Malaise and headache were common at the onset, but fever was exceptional. About a third had cough, usually unproductive. Postnasal discharge was uncommon; so were complications in the form of mild sinusitis or tracheitis. In fact, the experimental colds were rather mild and of brief duration, usually less than 6 or 7 days. Some people reported worsening of symptoms after going home, possibly through exposure to secondarily infecting bacteria. Many subjects receiving known infective material developed symptoms suggesting to them that a cold was developing, but this soon aborted. Such symptoms were not reported by the controls. We therefore suspect that in nature many colds abort spontaneously. The symptoms in our experimental colds were much the same as in the spontaneous colds detected or developing in 71 subjects during their quarantine period; this fact suggests that the disease we have studied possibly represented one of the commonest types of infection in the community. In short, even though there are other agents which produce a picture like that of the common cold, we are likely to find a large part of the total of colds forming "a" disease. Whether there exist different serological types of the causal agent, as with influenza viruses A and B, is an open question.

WHAT IS THE CAUSAL AGENT AND WHAT ARE ITS PROPERTIES?

The syndrome just described has been produced by intranasal inoculations in 60% of our volunteers; bacteria-free filtrates through gradocol membranes (average pore diameter 0·7μ) have been almost or quite as effective as unfiltered washings. Such colds have been transmitted in series through four persons and are almost certainly due to a multiplying agent, which we feel is to be regarded as a virus. The incidence of colds as a result of these inoculations has not demonstrably been affected by the age or sex of the subjects. The infectivity is reduced by dilution 1 in 100; with such diluted material 6 colds were produced in 22 subjects

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TABLE II—RESULTS OF TESTING FILTRATES OF COMMON-COLD WASHINGS ON VOLUNTEERS

Average pore diameter (mμ)	Number tested	0	±	+
410	3	1	0	2
310	15	5	1	9
230–220	8	7	0	1
140–120	20	10	1	9
68–57	22	20	1	1

+, definite cold; ±, doubtful mild cold; 0, no cold.

(27% positive). Washings diluted 1 : 10,000 were inactive (three attempts). Virus filtrates suffered no demonstrable loss on storage in sealed ampoules in dry ice (−76°C) for two years. At −10°C they survived at least 27 days and at 4°C for at least 3 days; longer periods were not tested.

The size of the virus has been estimated by filtration through Elford's gradocol membranes. In every case at least 10 ml. was filtered to ensure saturation of the membrane and sufficient broth was used as diluent to keep the absorption of virus at a minimum. The results of testing these filtrates on volunteers are shown in table II.

These filtration results suggest that the common cold virus is considerably smaller than the influenza virus. How much smaller is difficult to say, because the filtrates were almost certainly of low titre, and it depends on the significance of the one cold observed in the group of volunteers infected with 68–57mμ filtrates. If this was a genuine experimental cold, the most probable size is about 20mμ or less. If, on the other hand, the cold was only apparently induced by that filtrate, the most probable size is 40–50mμ.

As already mentioned, the first object of the Salisbury unit was to find a laboratory tool with which to study the virus. Successful cultivation of the virus in fertile hens' eggs seemed to offer most hope of attainment. Four commonly used techniques were available to us. For inoculations on chorio-allantoic membranes we used 462 eggs, and for amniotic inoculation 432; 28 volunteers were used for testing the membrane "cultures," and 54 for those in the amniotic cavity. 272 eggs were used for attempted cultivations in the allantoic sac, and the resulting fluids were tested in 99 volunteers. Yolk-sac cultivation was tried in 230 eggs, and 65 volunteers were used for testing. No evidence of successful cultivation was obtained, nor even of survival for one passage. At first we hoped we had succeeded; 15 mild colds and 20 doubtful ones were produced with our "cultures." Uninoculated embryonic membranes and fluids were, however, not so innocuous as serum-broth had proved, for they produced 8 mild and 8 doubtful colds in 57 attempts. The incubation period for these was the same as for our other experimental colds; we felt it possible that we might be activating with a mild irritant a cold-agent carried by some persons.

Our failure to cultivate a cold virus in fertile eggs contrasts with the published reports of Kneeland et al. (1936), Pollard and Caplovitz (1947), and Topping and Atlas (1947). Possibly some or all of these workers were dealing with a different infectious agent from ours; this seems especially likely from the account of the clinical features given by Topping and Atlas. Our techniques have, so far as we are aware, duplicated those of American workers. We have also tried to infect with virus several species of animals, using for most of them the technique of "blind passage," which involves passage of possibly infectious material through several animals in series, despite the absence of visible lesions. We used mainly intranasal but also intracerebral, intravenous, corneal, intraocular, and intratesticular inoculation. We did not, for obvious reasons, test chimpanzees, the only known susceptible species other than man. We used rabbits, guineapigs, rats, mice, cotton-rats, hamsters, voles (*Microtus arvensis*), grey squirrels, ferrets, kittens, pigs, hedgehogs, and several species of monkey—baboons (*Papio papio*), a sooty mangabey (*Cercocebus fuliginosus*), brown capuchins (*Cebus fatuellus*), green monkeys (*Cercopithecus æthiops sabæus*), and a red patas monkey (*Erythrocebus patas*). No symptoms or lesions attributable to the common cold were produced in any species, nor did the virus persist even for one passage in the ferret, mouse, hedgehog, hamster, cotton-rat, or capuchin monkey.

Many workers have failed to find in cold secretions cultivable bacteria likely to be of significance. Some bacteriologists nevertheless believe that pneumococci or other bacteria may cause some colds. This idea could be tested without difficulty; if bacteria-free filtrates of washings from such colds should induce colds transmissible in series, it would seem likely that the bacteria present were merely secondary invaders, arriving with special promptitude.

HOW LONG DOES VIRUS PERSIST IN OR OUT OF THE BODY?

Clinical opinion supports the view that colds are especially infectious in the early stages. Our experience confirms this; indeed we have found virus in nasal secretions well before symptoms develop. Volunteers were infected intranasally, and the nasal spaces were washed out 12, 24, 36, and 48 hours later. Only on the last occasion were symptoms present when washings were taken. The washings were inoculated into volunteers; no virus was detected in the 12-hour washings; but good "takes" were obtained with the 24-, 36-, and 48-hour specimens—i.e., virus was present, probably plentifully, 24 hours before the cold showed itself.

Direct tests for persistence of virus after a cold are incomplete. Epidemiological evidence, however, suggests that virus dies out rapidly from a small community. Colds normally cease to trouble an isolated group, such as a band of arctic explorers, soon after they have left civilisation behind. According to Paul and Freese (1933) colds become infrequent in Spitzbergen within a fortnight of the departure of the last ship at the end of October, and remain very rare until an epidemic is provoked by the visit of the first ship at the end of the following May. Dr. E. J. S. Woolley informs us that in Tristan da Cunha visiting ships bring with them epidemics of colds, but that these are brought only by ships from Cape Town, the voyage from which lasts not more than 12 days. Ships coming from Panama round Cape Horn do not bring colds. Perhaps the virus normally dies out within a few weeks.

Experiments of ours at first sight conflict with such a view. Nasal washings from normal persons without colds have, in tests on 28 persons, produced 6 colds, all mild ones. It has not yet been proved by serial transfer that these are caused by a virus. Epidemiological data from Spitzbergen and elsewhere show that ships may bring colds to a community even though those on board have no colds. The existence of normal carriers is therefore suggested. Possibly in a large community virus keeps going by passage from man to man, not necessarily producing symptoms in all whom it visits, and tending to die out if it is not from time to time reinforced in its activity by finding a susceptible victim.

We have no direct evidence that cold virus can survive long outside the body. Influenza virus certainly can persist for a fortnight in dust (Edward 1941). There is an exception to the rule that Arctic explorers do not catch colds in polar regions. Several records attest that, when bundles of clothes or blankets which have been stored for many months are opened, an epidemic

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of colds may result. It would be important to know whether such were really virus colds.

ARE COLDS ALWAYS "CAUGHT"?

That infection is often caught from people with colds cannot be doubted. Attempts to study the matter experimentally are difficult because the incidence of natural contact infections is so low. In one trial at Salisbury three pairs of volunteers were infected. Two of these pairs were chosen as "donors," and normal people ("recipients") were exposed to them by remaining together in one room for about 10 hours. The recipient pairs thereafter remained in isolation. Exposure of 8 persons was in the pre-symptom stage of the donors (24–34 hours after infection); 11 others were exposed to full-blown colds (72–82 hours after infection). Only one unequivocal cold developed, and that after 5 days, in a person exposed to pre-symptom colds; 5 other "recipients" had doubtful symptoms which we could not class as positive; 13 remained symptom-free. This result confirms a report by Kerr and Lagen (1933–34); these workers failed to obtain evidence of natural transmission of colds. Long et al. (1932) record the catching of a cold by two chimpanzees from a person who was incubating one and developed it next day. Reasons are given below for thinking that in all our transmission studies we are attempting with an enormous dose of virus to overcome a fairly high resistance. Because colds do not pass readily to normal resistant people, it does not follow that they do not do so to people who are for some reason vulnerable.

Opinions differ about the rôle of cold feet, draughts, and so forth in inducing colds. Experience in the Arctic suggests that such factors do not act in the absence of the infective factor. It could well be, however, that in people temporarily carrying a virus various happenings could upset a precarious host-virus equilibrium and lead to the appearance of a cold.

BY WHAT MEANS DOES VIRUS SPREAD?

The old idea of droplet infection has in some quarters lost popularity in favour of Wells and Wells' (1936) conception of droplet-nucleus infection. They conceive that many small particles leaving the nose or mouth evaporate instantaneously to a diameter of less than 10μ and remain suspended in the air for an hour or more. Probably only a minority of such nuclei will carry micro-organisms, and these will commonly be exposed to the lethal effects of daylight. In any case the quantity inhaled will be infinitesimal. This infinitesimal dose may well suffice to infect, let us say, a child fully susceptible to measles. Where, however, we are dealing with a population having a fairly high resistance to a particular infective agent, it seems likely that coarse droplets, giving a "direct hit" from a sneeze, or some other method of transferring a large dose, will be more important. If this is so, the prospects of diminishing the incidence of colds by air sterilisation are not very rosy.

Studies in collaboration with the Medical Research Council's air hygiene unit at Salisbury show that bacteria can be dispersed into the air in enormous numbers when handkerchiefs are shaken or even handled. Though at present evidence is inconclusive, it is not unlikely that cold virus can become airborne in the same way. If so, there is much promise in recently developed techniques for impregnating handkerchiefs with disinfectants which will kill the organisms on the handkerchiefs and cut down by 95% the numbers which reach the air on shaking (Dumbell et al. 1947). Unpublished studies show the enormous possibilities of spreading infection by indirect manual transfer—from nose to handkerchief to fingers to anything touched and to someone else's fingers, handkerchief, and nose. In this connexion we recall an observation by Bliss and Long (1933): 5 chimpanzees developed colds 48 hours after eating food prepared by a food-handler in his 2nd day of a severe cold. This person had no direct contact with the apes or their attendants.

HOW COULD COLDS BE ACTIVATED?

One suspects that, if activation of a cold in a virus carrier is possible, it probably operates through some local change in the nasal mucosa. Mudd and Grant (1919) using a thermopile, found that chilling the body caused, by reflex vasoconstriction, a fall of temperature in the nasopharynx. This was not quickly recovered from. The lining of the upper respiratory tract is apparently covered by a sheet of mucus continuously moving backwards. Local drying up of this is a possible factor leading to a temporary breakdown in defence against infection. Several observers attest that allergic reactions in the nasal mucosa to pollens or other allergens may be followed by what seems to be a genuine infectious cold.

WHY ARE COLDS SEASONAL?

We all associate colds with cold weather, but data are scanty and do not all agree as to how much commoner colds are in winter than in summer. Attempts to relate the incidence of cold to temperature, rainfall, humidity, and sunshine have not been convincing. The climatic changes associated with an increase of colds may vary from country to country. Thus the onset of cold weather heralds a wave of colds in temperate climates; elsewhere monsoons may determine the issue. In the Virgin Islands in the West Indies (Milam and Smillie 1931) a wave of colds may come in December, when the temperature is only a few degrees below that at midsummer. Unknown factors may tend to make the disease inherently periodic, and climatic changes, varying from country to country, tend to keep that periodicity in harmony with an annual cycle. One must also bear in mind that people's habits vary through the year; in the winter they crowd more together indoors, whereas in summer many people get a change to another environment. If this involves a holiday in the open air, particularly away from the "madding crowd," the general health may improve but resistance to colds may simultaneously fall.

WHY DOES RESISTANCE TO COLDS VARY?

General experience tells us that resistance to colds does not last long. Dingle and his fellow workers (Commission on Acute Respiratory Diseases 1947) inoculated 5 volunteers with a cold virus and produced colds in 4 of them. Meanwhile they stored some of the same virus in the cold until, 19 days later, these colds had cleared; they then used the stored virus to challenge the immunity of the same 5 persons. Again 4 out of 5 developed colds—the one who had resisted the first inoculation was this time a victim. Such a result need not mean that immunity to colds is necessarily quite so short in natural circumstances.

As already indicated, the dose of virus received when undiluted washings are given intranasally must be thousands of times as big as any conceivable "natural" dose. Even so, about 40% of persons prove resistant, though hardly any of them claims to be free from colds throughout the year. Our data are not yet big enough to satisfy us, but so far they do not suggest that resistance of our volunteers to colds evidently depends on the time elapsed since their last cold. Knowledge of herpes simplex, another recurrent virus disease, renders it arguable that resistance to colds may be independent of variations in antibody level (Burnet 1939). (Those subject to recurrent herpes simplex have high antibody titres; those who never have it are immune despite a lack of antibodies.)

Nowadays one has to consider the "interference phenomenon" in discussion on resistance to virus.

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Possibly the carrying of one, perhaps avirulent, virus in the nose may be associated with resistance to other viruses. It would be of interest to try to relate the presence of a "carried" cold virus in normal people to their resistance to inoculation with cold filtrates from another source.

We are quite without evidence as to whether serological types of cold viruses exist. If immunity does not depend on antibodies, the question may be irrelevant. One could argue that, if immunity to the virus is so brief, evolutionary factors might not tend to antigenic diversity. Stories that travellers from abroad develop colds on reaching England may be related less to contact with a strange virus here than to infection through close contact with fellow passengers on board ship before it reaches port.

Many observers attest that resistance to colds varies in individuals from year to year (Gafafer and Doull 1933, Browning 1942) and for no apparent reason. This fact incidentally has much to do with the reputations, transient though these usually are, of most cold preventives.

An interesting possibility has emerged from analysis of our records at Harvard Hospital. With a 60% "take" among volunteers living in pairs one can calculate the probable distribution of colds in each flat, whether two positives together (++) two negatives (00) or one of each kind (+0). In practice members of a pair tend to react alike, the +0 result being much below expectation. Most pairs come together, either as married couples or friends, at any rate from the same environment, and the tendency to react alike is seen particularly in such associates. It is conceivable that, if there is a cyclic variation in susceptibility to colds, close associates might tend to be in the same phase of the cycle. Such a cycle might depend on acquisition, temporary carriage, and ultimate loss of a virus from the nose. Our data are capable of alternative explanations, and this "phase theory" has no strong evidence in its support. We are, however, satisfied that the tendency of members of a pair to react alike is not likely to be due to cross-infection of one partner from the other.

We cannot help concluding that for certain studies our volunteers are too resistant and too variable in their resistance to be ideal subjects for experiment. We should be much better off if we had available Spitzbergenites assembled during April at a period when their susceptibility was probably low and uniform. Experimental work on colds is difficult. We are convinced that much of great value is still to be learnt simply by accurate observation and recording of happenings in suitable, particularly in isolated, communities, in the Arctic or islands and in ships.

CONCLUSION

It may be useful to consider the possibility that colds are due to a virus which, in a large community, is constantly passing from one person to another, usually causing no symptoms, often only abortive ones, and a real cold only when it finds a victim whose local resistance is for some reason at a temporary low ebb. From such a person it is dispersed in greater quantity. Few people harbour it for long; hence in isolated groups it commonly soon dies out. Such a conception is not proven, but is in harmony with known facts.

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HEALTH SERVICES BILL IN AUSTRALIA

FROM OUR AUSTRALIAN CORRESPONDENT

THE health minister on Nov. 24 introduced the long-awaited National Health Services Bill into the Senate. The outstanding feature is the proposal that the government should pay half the doctor's fee. This amount would be paid direct to the doctor in accordance with a "prescribed schedule of fees chargeable by doctors who participate."

Senator McKenna estimated that with full participation by doctors the medical-benefits scheme would cost about £A6 million a year and the dental scheme eventually about £A4 million. Both would be financed from the National Welfare Fund, with capital expenditure an additional charge to be appropriated by Parliament. Senator McKenna explained that the Bill was an enabling measure, giving only the broad outline of the proposed National Health Service. Details of the service and its administration are to be left to progressive development by regulations; this is regarded as the ominous phrase in the Bill, and it may prove the stumbling-block to its acceptance by the British Medical Association in Australia.

Senator McKenna emphasised that the government did not contemplate, nor did the Constitution permit, any nationalisation of doctors, dentists, or allied professions, and "faced with grave deficiencies in numbers of trained personnel, equipment, and buildings, the government realises that establishment of a complete health service must be achieved by gradual development."

GOVERNMENT POWERS

The Bill enables the Commonwealth:

To provide or arrange for medical and dental services, including general practitioner services, consultant and specialist services, ophthalmic services, maternity and child-health services, convalescent, aftercare, and nursing services, and medical and dental services in universities, schools, and colleges; and to establish and maintain hospitals, laboratories, health centres, and clinics.

To make payments to assist research and provide training courses in medical or dental science; to provide or assist in the provision of postgraduate training and scholarships in medicine and dentistry; to establish and develop courses of training in nursing, dental hygiene, radiography, radiation therapy, physiotherapy, and biochemistry; to undertake to develop and encourage measures for improvement of health and prevention of disease; to undertake the manufacture of medical and dental supplies, appliances, and equipment including visual and hearing-aids if adequate supplies are not assured at a reasonable price from other sources.

The medical benefit scheme would be begun as soon as possible, and extended as rapidly as circumstances permitted to include the various classes of specialists on terms similar to those of general practitioners.

It is proposed to pay a full-time salary to doctors in remote country areas, and to full-time specialists

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such as pathologists and radiologists in hospitals. Sessional fees would be paid to other specialists, and salaries to medical superintendents and full-time hospital staff. Senator McKenna assured Parliament that the scheme would involve no interference with the present practice of medicine. It would not involve any disturbance of the doctor-patient relationship.

In making his claim for payment the doctor will have to disclose, among other things, each item of service for which payment is claimed. The government proposes to write to a percentage of all patients requesting them to state whether they received a certain service from a certain doctor on a certain day. To prevent abuse by over-charging, doctors are to keep clinical records of all their patients. Doctors will also have to keep accounts according to a standard form laid down by the federal health department, to which complete records of treatment must be rendered before payment is made.

HEALTH CENTRES

The Commonwealth, recognising the value of group practice, propose to establish a number of health centres in different areas. These would correspond in function to the surgeries of the larger medical partnerships of the present day, and would provide general-practitioner and specialist services and diagnostic facilities. The Bill authorises regulations to pay compensation to a practitioner who makes his services available exclusively for the National Health Service where establishment of such a health centre results in loss arising from diminution in value of his private practice.

The Bill also authorises compilation and publication of lists of doctors and dentists recognised as specialists. Regard may be had to any similar list prepared by a State authority or professional body as well as to the advice of appropriate advisory committees to be established. The object is to establish a list of persons who may be regarded for the purposes of the Bill as entitled to receive or charge fees prescribed for specialist or consultant services.

DENTAL SERVICES

Dentists would also come under the scheme, and the government would pay half the fee. Although handicapped by a serious shortage of dentists—two or three times the existing total of 3000 registered dentists would be required for a full and satisfactory service to all classes and ages—the government intend to improve facilities for dental service.

The dental scheme would be developed through a directorate of dentistry on three lines:

1. Public education in the principles of dental hygiene.

2. Attack on the problem of providing regular treatment for all children, using existing facilities and special dental clinics; in rural areas mobile dental surgeries would be necessary. The shortage of dentists would severely limit the age range of the scheme at its inception, but eventually a full service for all children would be available. The government is examining the New Zealand scheme of using specially trained dental hygienists for limited activity in treating school-children, and would consider training hygienists in Australia if necessary.

3. Extension of dental services to isolated areas by travelling clinics maintained by a salaried staff.

OPINION

"Shellbacked old conservatives" was the description applied by Mr. J. B. Chifley, the Prime Minister, to the people who claimed to represent the B.M.A. and who refused to coöperate in national health and free medicine schemes. "They don't want anything changed," he said. "They want the profession to remain as it is. Well, it's not going to remain as it is. If the government cannot get the coöperation of the B.M.A. the government will have to train its own doctors. Proper treatment is now too expensive for the average man and woman." Mr. Chifley added that inevitably big centres would have to be established where people for a fee could be examined by specialists and where they could obtain a card which would give any doctor in the world the complete story of their condition. "Until we have these centres we won't be able to get over the expense of medical attention."

The first step taken by the federal council of the B.M.A. was to ask for a commission of medical men to administer the Act. It was intended that the corporation should be non-political, and similar to the Australian Broadcasting Commission. The minister rejected the request and wanted the B.M.A. to agree to the details of the scheme being placed in the hands of a joint committee representing the doctors and the Commonwealth health services.

The main objection of the B.M.A. federal council is that it is contrary to policy to coöperate in a service controlled by a government department. The council argues as follows:

The regulation-making provisions, which would enable the whole medical profession, both present and future, to be brought under the control of the government, renders the Act in its present form unacceptable to the profession. All essential conditions of the service should be stated in the Act.

The medical profession refuses to make available to any third party, lay or medical, the clinical records of patients as part of the machinery for patients to obtain medical benefits under the National Health Services Act.

The right of any member of the public to obtain medical benefits in respect of a medical service received should not depend on the existence of any arrangement, agreement, or contract between the doctor providing the service and the government.

The willingness of any doctor to coöperate in the machinery for enabling some of his patients to obtain medical benefits should not debar him from entering into private arrangements with patients to the exclusion of the government scheme, provided such arrangements are acceptable to both parties.

The medical profession is unwilling to undertake the clerical work and liabilities involved in acting as "agent for the patient" in obtaining medical benefits, and insists that payment by the refund system be included in the scheme.

The Commonwealth government should pay the whole cost of the non-hospital medical service to old-age and invalid pensioners, and to people registered as unemployed over long periods, upon application being made by the patient.

The institution of experimental health centres, as envisaged in the Act, under the control of the government is unecessary and undesirable as replacing private doctors by government-employed doctors.

The medical profession refuses to admit the right of the government to fix a fee of which it pays only a part, and therefore demands that a scale of benefits and not a scale of fees be laid down.

The medical profession approves of its representatives—the full B.M.A. federal council—joining with representatives of the government in a joint committee to consider certain details of the government's proposals, provided that the committee should not function until agreement has been reached upon the general principles of the scheme.

The medical profession has no objection to the government paying a portion of the fees charged to patients provided that this portion is paid direct to the patient.

At a meeting of members of the New South Wales branch of the B.M.A. in Sydney on Nov. 26, fear was expressed that doctors' surgeries would be crowded with minor ailments. The meeting was told that it was a sickness scheme, not a health scheme. Australia was 18,000 hospital beds short of requirements, and it would cost £A40 million to remedy the position. The Queensland

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branch holds to four points: (1) the patient-doctor relationship must be maintained; (2) the patient must be free to choose his own doctor; (3) a doctor must be free to practise where he chooses; and (4) all negotiations must be with the B.M.A. and not with individuals.

The government has chosen the last few days of the present sitting to rush through the Health Bill. It is now realised throughout Australia that the "free medicine" Act is a dead letter. Even the general public is apathetic to its death. The approach to the doctors on the free medicine scheme was rather too totalitarian to be successful. The Australian public realises that the medical profession has always acknowledged that the best medical attention should be at the disposal of every person without regard to the individual's financial resources.

NEW YEAR HONOURS

THE list of New Year Honours, announced last week, contains the names of the following members of the medical profession:

Baron

Sir JOHN BOYD ORR, D.S.O., M.C., M.D., D.SC. Glasg., LL.D., F.R.S.
Lately director-general of the Food and Agriculture Organisation of the United Nations.

P.C.

Miss EDITH SUMMERSKILL (Mrs. Samuel) M.R.C.S., M.P.
Parliamentary secretary, Ministry of Food, since 1945.

G.B.E.

Sir WILSON JAMESON, K.C.B., M.D. Aberd., F.R.C.P., K.H.P.
Chief medical officer, Ministry of Health and Ministry of Education.

K.C.V.O.

Sir WILLIAM GILLIATT, C.V.O., M.D., M.S. Lond., F.R.C.P., F.R.C.S.
President of the Royal College of Obstetricians and Gynæcologists.

Knights Bachelor

HENRY COHEN, M.D. Lpool, F.R.C.P., J.P.
Professor of medicine, University of Liverpool.

HUGH ERNEST GRIFFITHS, C.B.E., M.S. Lond., F.R.C.S.
Surgeon, Albert Dock Hospital, London; for services in the industrial rehabilitation of disabled persons.

SYDNEY ALFRED SMITH, C.B.E., M.D. Edin., F.R.C.P.E.
Dean of the faculty of medicine and regius professor of forensic medicine, University of Edinburgh.

C.B. (Military)

Major-General FREDERICK HARRIS, C.B.E., M.C., M.B. Dubl., K.H.S.

Surgeon Rear-Admiral LIONEL FREDERICK STRUGNELL, M.B. Lond., K.H.P.

C.M.G.

ARTHUR BARTON PILGRIM AMIES, D.D.SC. Melb., F.R.A.C.S., L.R.C.P.E.
Professor of dental science, University of Melbourne.

THOMAS AITKEN AUSTIN, L.R.C.P.I.
Director of medical services, Uganda.

RICHARD BRUNEL HAWES, M.B. Lond., F.R.C.P.
Consulting physician to the Colonial Office.

MONTAGU TRAVERS MORGAN, M.C., M.D. Lpool.
Medical officer of health, Port of London.

C.B.E. (Military)

Surgeon Captain ROBERT WALSH MUSSEN, M.D. Belf., M.R.C.P., R.N.

C.B.E.

WILLIAM ARTHUR BULLOUGH, M.B., M.SC. Manc.
Medical officer and school medical officer for Essex.

JOHN BURTON CLELAND, M.D. Sydney.
Formerly professor of pathology, University of Adelaide.

Mrs. EMILY HANCOCK MCKINNON, M.B. N.Z., L.R.C.P.I.
Of Dunedin; for services in the field of medicine and welfare of women.

NORMAN MANSON, M.B. N.Z.
Warden, Hospital of St. John, Jerusalem.

WILLIAM BENTLEY PURCHASE, M.C., M.B. Camb.
Coroner for the Northern district of London.

WILLIAM ROBERTS, M.D.
Medical superintendent, Grace Hospital, Newfoundland.

O.B.E. (Military)

Major STEPHEN MACKENZIE, M.R.C.S., R.A.M.C.

Wing-Commander SIDNEY RICHARD CARLYLE NELSON, M.D. Alberta, R.A.F.

O.B.E.

Mrs. MARGARET MARY BASHAM, M.B. Edin.
County director, Monmouthshire branch, British Red Cross Society.

GEORGE FREDERICK BAXTER, M.R.C.S.
Senior surgeon, Public Hospital, Kingston, Jamaica.

ERIC HATTAWAY BRIDGMAN, M.B. N.Z.
Superintendent of Rotorua Hospital.

JOHN CHARLES CALLANAN, M.D. Dubl.
Director of medical services, Swaziland.

Miss CHARLOTTE ANN DOUGLAS, M.D. Glasg., F.R.C.O.G.
Medical officer, Department of Health for Scotland.

CHARLES EDWARD ETHERIDGE, M.B. Lond.
Admiralty surgeon and agent, Whitstable.

CYRIL FRANCIS FERNANDO, M.D. Lond.
Medical officer and physician, General Hospital, Colombo.

GEORGE GIGLIOLI, M.D. Pisa, M.R.C.P.
Honorary Government malariologist, British Guiana.

RICHARD MURCHISON MORRIS, M.D. Lond.
Medical director and secretary for health, Bulawayo, Southern Rhodesia.

Wing-Commander HAROLD BURNET PORTEOUS, M.B. Edin., R.A.F. retd.
Medical officer, Board of Customs and Excise.

ERNEST ALBERT HAROLD RUSSELL, M.B. Adelaide.
Consulting obstetrician, Queen Victoria Maternity Hospital, State of South Australia.

O.B.E. (Honorary)

FRANCIS AKANU IBIAM, M.B. St. And.
Medical practitioner on the staff of the Church of Scotland Mission, Nigeria.

LOUBE MARY-MADELEINE LENGAUER.
Medical officer, Leprosy Control, Nigeria.

M.B.E.

Mrs. OLGA KONSTANTINOVNA ABBOTT.
Physician, Ethiopian Vice Ministry of Health, Addis Ababa.

JOSEPH GALEA, M.D. Malta.
Medical officer of health, Malta.

". . . In many of us the proposal now under consideration to combat crime by means of a national campaign of propaganda and moral exhortation strikes a chill in the heart. In many spheres of life we have given up exhortation and turned for aid to scientific inquiry and technique. . . . Advance in medicine has come through our learning how to aid the body's natural resistance to disease and potential for healthy development. Advance in social health will come when we have learnt how to assist man's natural capacity for coöperation and how to provide the optimum conditions for its growth. Instead, then, of using time and energy in propaganda campaigns exhorting people to work harder or to be more law-abiding, let us institute measures more in keeping with the experience of the twentieth century. First, let us use in our preventive and therapeutic measures the very considerable amount of scientific knowledge already to hand. Secondly, let us promote research. In the case of crime, research is especially needed into methods for the rehabilitation of the persistent delinquent and above all into the origin of this condition and into measures for its prevention.—Dr. JOHN BOWLBY, *Times*, Dec. 20.

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Public Health

FOG AND MORTALITY

W. P. D. LOGAN
M.D., B.Sc. Glasg., D.P.H.
ASSISTANT MEDICAL STATISTICIAN, GENERAL REGISTER OFFICE

THE dense fog that enveloped London and much of the country during the closing days of November, 1948, established a record, not for density but for duration.

TABLE I—DEATHS REGISTERED IN LONDON (ADMINISTRATIVE COUNTY) DURING WEEKS 44–51

Year	Week No.							
	44	45	46	47	*48*	49	50	51
1945	593	639	638	707	739	734	907	979
1946	654	742	780	753	778	727	887	945
1947	739	771	742	799	721	861	817	779
1948	811	801	846	779	*1019*	944	891	738

Commencing in London on the night of Friday, Nov. 26, it persisted until Wednesday, Dec. 1. The disruption of transport that it occasioned received ample comment in the press; but less mention was made of the toll in life that it might be exacting.

TABLE II—DEATHS FROM SELECTED CAUSES REGISTERED IN LONDON (ADMINISTRATIVE COUNTY) DURING WEEKS 44–51 OF 1948

Cause	Week No.							
	44	45	46	47	*48*	49	50	51
Respiratory tuberculosis	33	36	44	36	*46*	45	37	34
Influenza	1	2	3	2	*3*	4	2	2
Bronchitis	63	57	68	73	*148*	103	88	55
Pneumonia	32	42	46	29	*73*	71	67	51
Road traffic accidents	5	8	9	3	*9*	6	2	4
Old age	8	7	7	8	*5*	13	9	8
Myocardial degeneration	95	97	125	102	*133*	135	103	79
Cancer of respiratory system	35	48	30	31	*42*	34	20	20
Cancer of other sites	135	119	135	118	*148*	115	146	123

The fog occurred mainly during the first half of the week ended Dec. 4, the 48th week of the year. The total weekly deaths from all causes registered in London during weeks 44–51 of 1948 and of the three previous years are shown in table I.* The sharp rise in deaths registered during the week of fog stands out clearly, 20–30% more deaths being recorded in that week than in each of the 4 previous weeks. The effect continued into the 49th and perhaps the 50th week of the year.

TABLE III—DEATHS FROM BRONCHITIS AT VARIOUS AGES, REGISTERED IN LONDON (ADMINISTRATIVE COUNTY) DURING WEEKS 44–51 OF 1948

Age (years)	Week No.							
	44	45	46	47	*48*	49	50	51
<1	2	..	4	..	*2*	4	7	1
1–14	2	..	..	..	*2*	1	1	..
15–44	..	2	1	6	*4*	5	4	4
45–64	11	11	13	8	*32*	19	20	8
65+	48	44	50	59	*103*	74	56	45

TABLE IV—DEATHS FROM PNEUMONIA (ALL FORMS) AT VARIOUS AGES, REGISTERED IN LONDON (ADMINISTRATIVE COUNTY) DURING WEEKS 44–51 OF 1948

<1	7	4	12	4	*6*	19	12	13
1–14	1	..	2	3	*2*	4	4	1
15–44	..	..	2	1	*5*	..	1	..
45–64	6	8	6	4	*19*	11	11	9
65+	18	30	24	17	*41*	37	39	28

Table II shows the number of deaths ascribed to various causes during these 8 weeks. As was to be expected, much of the increased mortality was due to respiratory infection. Registered deaths due to bronchitis and to pneumonia more than doubled during the 48th week, deaths from most other causes being little if any higher than in the previous 4 weeks. There was, however, some increase in deaths from myocardial degeneration and cancer.

The ages at which bronchitis and pneumonia caused death are shown in tables III and IV. During the fog week there was no increased mortality from either disease at ages under 45. The increase was numerically greater above the age of 65 but proportionately greater in the 45–64 age-group. In the next 2 weeks (49 and 50) bronchitis deaths returned practically to their normal level, but not so the deaths due to pneumonia especially among the elderly. The registered mortality from pneumonia in infancy was not increased during the week of fog but rose to a high level in the following week.

* The figures in this and the subsequent tables are taken from the Registrar-General's weekly return.

Uncooked Meat for Animals

The National Veterinary Medical Association has issued a warning against buying uncooked meat at pet food shops. Some of this meat, says the association, may have been condemned as unfit for human consumption, on account of its being affected with tuberculosis or other disease. "There is an obvious danger of dogs and cats contracting disease from this source unless the meat is thoroughly cooked; and the danger to animal-owners handling such meat before it is cooked is by no means negligible. Where such meat has to be handled raw, it is advisable to wash the hands thoroughly afterwards." It is suggested that shops selling meat intended for dogs and cats should sterilise it on the premises by boiling.

Statistical Reviews

THE YEAR 1943

Part 2 of the Registrar-General's Statistical Review for 1943,[1] now published, shows that during that year in England and Wales the improvement in the birth-rate since the record low figure in 1941 was maintained; the fall in the stillbirth-rate continued; and the number of marriages was the lowest for 17 years.

Births.—There were 684,334 live births, representing a birth-rate of 16·2 per 1000 total population. This maintained the improvement seen in 1942 when the corresponding figures were 651,503 and 15·6 respectively. The rate for 1943 was the highest since 1930 when it was 16·3. (The rate further increased to 17·7 in 1944, fell to 15·9 in 1945, and again increased to 19·2 in 1946 and 20·6 [provisional] in 1947.)

Of the live births 43,709 (6·4%) were illegitimate compared with 36,467 (5·6%) in 1942 and an average of 4·3% for the ten years 1930–39. (In 1945 this percentage was 9·3, in 1946 it was 6·6, and in 1947 it was 5·3.)

Stillbirths numbered 21,262, representing a rate of 30 per 1000 total live and still births, compared with a rate of 33 in the previous year. (This marked decline in the rate is continuing; the provisional rate for the third quarter of 1948 reached a new low record of 22·6.)

Marriages.—These numbered only 296,432 in 1943, giving a rate of 14·0 per 1000 total population. This was the lowest number for any year since 1926, when it was 279,860 with a rate of 14·3. The most popular age for marrying was 22 for men and 21 for women, the mean ages at marriage being 29·1 for men and 26·1 for women.

Fertility.—44·6% of all legitimate maternities in 1943 were first confinements; 27·0% were to mothers who had had one previous child (surviving, dead, or stillborn); and 12·4% to mothers who had had two previous children. There were 8259 confinements resulting in

1. The Registrar-General's Statistical Review of England and Wales, 1943, Part 2 (Civil). H.M. Stationery Office. Pp. 92. 2s.

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multiple births, 8193 being twins, 62 triplets, and 4 quadruplets. Some 64,000 (about 22%) of the first maternities occurred within 11½ months of marriage, and of these about 35,000 occurred within 8½ months of marriage.

THE YEAR 1946

Part 1 of the review for 1946 [2] shows that the number of deaths registered in that year was 492,090, giving a crude death-rate of 12·0 per 1000 civilian population. This was the lowest crude rate since 1938 when the corresponding figure was 11·6. The comparative mortality index (which allows for the changing sex and age structure of the population and expresses the mortality of each year in relation to that of 1938) was only 0·881 in 1946, compared with 0·893 in 1945 and 1·000 in the base-year 1938. Thus 1946 was an even healthier year than 1945 and was the best recorded up to that time.

Infant and Maternal Mortality.—Infant mortality in 1946 was the lowest recorded up to that time, being 42·85 per 1000 related live births compared with 46·00 in 1945 and the previous lowest rate of 45·44 in 1944. Maternal mortality (excluding that due to abortion) also continued to decrease from the previous lowest figure of 1·47 in 1945 to 1·24 per 1000 total live and still births in 1946.

Epidemic Diseases.—The rapid decrease in the number of deaths from diphtheria since the introduction of the immunisation campaign was again emphasised by a new record low figure of 455 civilians in 1946, compared with 694 in 1945 and 2622 in 1941. The death-rate of children under 15 years of age from this cause was only 40 per million. The under-15 death-rates from scarlet fever and measles were also the lowest recorded, being 3 and 22 per million respectively. The rate of 91 deaths from whooping-cough per million children under 15 was an increase on the low figure of 79 in the previous year but was still appreciably lower than the pre-war average.

Respiratory Tuberculosis.—There were 19,365 deaths (including non-civilians) from this cause, compared with 20,013 in 1945 and 23,660 in 1940. The mortality index of 0·927 was the lowest ever recorded, the previous lowest being 1·000 in 1938.

Cancer.—The mortality index for cancer in 1946 was 0·986—a slight increase on the low figures of 0·982 and 0·975 in 1945 and 1944. The improvement shown by the progressive decline of the index for cancer in females between 1936 and 1945 was arrested in 1946 when the index was 0·948 compared with 0·936 in 1945. The index for males, which has increased, though less regularly, from 1·001 in 1936, was 1·019 in 1946 compared with 1·025 in 1945. The increase in mortality from cancer of the lung of both sexes seen in previous years continued.

Diabetes.—The mortality index for diabetes which has shown a progressive and regular decrease for both sexes since the record high figure of 1·059 in 1940, was only 0·650 in 1946—the lowest ever recorded.

2. The Registrar-General's Statistical Review of England and Wales, 1946, Part 1 (Medical). H.M. Stationery Office. Pp. 351. 6*s*.

Notification of Infectious Diseases

ENGLAND AND WALES

	Week ended Dec.			
	4	11	18	25
Cerebrospinal fever	33	39	35	22
Diphtheria	131	144	124	100
Dysentery	64	69	54	30
Encephalitis lethargica	...	...	...	...
Measles, excluding rubella	8562	10,094	9800	8959
Ophthalmia neonatorum	47	36	58	18
Paratyphoid fever	10	3	1	3
Pneumonia, primary or influenzal	897	1027	1082	792
Polioencephalitis	9	1	1	2
Poliomyelitis	51	35	28	17
Puerperal pyrexia	108	98	95	78
Scarlet fever	1527	1410	1426	1154
Smallpox	..	..	..	..
Typhoid fever	4	4	7	4
Whooping-cough	2562	2522	2471	1791

In England Now

A Running Commentary by Peripatetic Correspondents

THE second Test opened at Johannesburg with the temperature in the nineties. As we backed through a gully into a parking place a familiar grating noise told me that my M.G. had grounded its tail. This often happens, for the M.G. is the achondroplasic of the motor world, and I was not surprised. When, however, a second or two later the engine spluttered to a stop and a sinister hissing sound came from the rear I was taken somewhat aback. Investigation disclosed that the external os of the exhaust was acutely obstructed by a mass of tarmac rendered glutinous by the heat and scraped up from the road. An emergency curettage with a screwdriver relieved the obstruction sufficiently for flatus to pass comfortably and all was well.

Cyril Washbrook treated us to some magnificent cricket. The ease—almost negligence—with which he stroked the ball gently to unoccupied parts of a field cunningly set and frequently altered by Dudley Nourse was delightful to watch, as was the way he and Hutton stole short runs even in the hottest hours after lunch. Begbie's catch which dismissed him was a worthy end to his innings; a high ball, deep on the leg and right in the eye of the sun. The ovation Washbrook got should be some recompense for his dismissal five runs short of his double century.

* * *

Do you want a perfect means of escape for about two hours a week from the daily trials of the National Health Service? Then form a choral society, work your way through five of Handel's oratorios with appropriate public performances, and finally try making perfect recordings of the finished product.

Having warmed ourselves up with *Samson*, *Solomon*, *Saul*, and *Judas Maccabæus* we decided to put on the *Messiah* as a Christmas piece in four churches and try to record the lot. One encounters so many assorted obstacles in this kind of venture that the mind becomes gradually conditioned to almost anything. Troubles ranging from tympani to temperament are always with us and a little medical knowledge often comes in handy. A few tablets of phenobarbitone in one pocket and amphetamine in the other, judiciously prescribed at the apt moment, may make all the difference between success and failure. A small lapse in the chorus may escape notice. but your soloists face the enemy alone.

Our first attempt at recording was grand fun. I will draw a veil over the preliminary tests in the morning. When we arrived at the church there was a requiem in progress and the body stayed behind after the mourners had departed. Feeling like tomb-robbers, we crept about installing mikes and recording gear in the choir loft and sacristy, connecting up unending yards of wire. As time was precious we devised a method of keeping *cave* on the corpse and emitting loud trumps on the organ when there was nobody within earshot. Unfortunately the deceased seemed to have an endless stream of respectful relatives, some of whom even took the lid off and peered inside. I had a lot of work to do, so I left the engineers to it and came back some hours later. All was evidently well, for all wiring was complete with a microphone lashed into position in mid-air beyond the choir screen. In their haste some primitive material had crept in. The echo side of the microphone was swathed in a vivid bandana handkerchief, while the stand was protected from vibration by what appeared to be an intimate female undergarment. I remember two ladies practising "He shall feed his flock" while the engineers tried to keep a pedal bourdon under control, and I can only hope that neither of them caught cold on the way home.

For the actual performance we had devised a system of signal lights, only to find at the last minute that they made horrible noises on the recorder when they were switched on; so a pull signal down the choir stairs was hastily arranged. I held one end and the assistant engineer the other. Between us were a dozen tenors and basses interwoven in the line at waist level. At times some of them were lucky to escape serious mischief from our frenzied tugs. Perhaps similar trouble caused

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Handel to specialise in male altos. But all went well. Of our pre-arranged signals, ranging from "Ready?" to "Abandon hope, all is lost!" we only had to use two; "Start" and "Finish." From the first "Comfort ye" to the last "Hallelujah!" time and pitch never failed, and as a tail-piece we played back an almost faultless rendering of the Hallelujah Chorus to an astonished congregation. Later the choir heard entranced the magnificent bass recording of "The people that walked in darkness" and the snap and sparkle of their thunderous entries in "Unto us a child is born." Of course, later listening brought reactive criticism; we found a tendency to premature accouchement by the tympanist and a bit where six of the sopranos scarcely had a child at all. But I must refute as entirely slanderous the suggestion by one of our teetotal members that our drummer ought not to have attended a church in that condition.

It was all enormous fun and a great success, but somehow, despite the new health scheme, I shouldn't care to exchange permanent places with Sir Malcolm Sargent.

* * *

A story now for DOCTOR GRIST
(See I.E.N. for Christmas Day)
Describing, I am glad to say,
A Case which his Successor missed.
In summer, on a tandem tour
With windy Dartmoor as a lure
We passed through Totnes; on the way
We saw, behind a one-hoss-shay,
An ambulance bedecked in white
Whose number-plate all clean and bright
Was surely quite a record odd one;
It bore the index-number BOD 1.

* * *

After six months of it one may perhaps be allowed to record a few impressions of the working of the Act. They are not particularly favourable. Patients seem to have resolved themselves into two groups quite independent of economic status. The first and very much smaller group comprises the more sensitive who, in many cases when they could justifiably call on the doctor's services, shrink from doing so from fear of adding to his work. The larger group consists of those who want all they can get, who clutter up surgeries, who demand visits rather than ask for them, and who press for needless specialist services. In a recent leader THE LANCET pointed to the crowding of surgeries as evidence for the need for a national health service. This may be partly true. But may it not also be partly due to a determination to get at least a shilling's worth in return for tenpence a week?

The lack of acceptance of trivial and temporary departures from health, notably among the young, coupled with an increasing lack of resignation to the disabilities inseparable from senility on the part of the aged, combine sometimes to engender feelings of resentment towards patients which, under the old relationship, were not there. Moreover, the number of *malades imaginaires* appears to be increasing, and whereas a rich country could afford a few of these tedious luxuries it is certain that a poor country cannot afford a large number of them.

Of the Act's manifold inconsistencies and administrative chaotics, which are remediable and may possibly in time be remedied, others have spoken and will doubtless continue to speak. I am concerned more immediately with the changed relationship of patient and general practitioner. In the old days the fact that one felt worthy of gratitude, whether or no it was forthcoming, was a soothing and warming thing. Now, the same degree of care and trouble is too often regarded as nothing more than the doctor's plain duty. Time was when we were held to be a learned profession; now, we have become little more than shopkeepers. No longer do we say to the new patient: "What is it that is troubling you?" Rather do we say: "What can I do for you?" and stand poised, pen in hand, ready to prescribe the aspirins, the wigs, the cod-liver oil, and the elastic stockings, or to write the formal certificate. Dignity and humanity are passing from us. How are we to get them back?

Letters to the Editor

NO ROOM AT THE HOSPITAL

SIR,—Lord Amulree in his letter of Dec. 25 goes to the heart of the matter. Dr. Marjory Warren and others have shown us the way out. It is up to the Ministry and the boards and management committees to apply their methods on an increasing scale. I am told that in this region there are approximately 4500 aged sick patients in public-assistance institutions. Can anyone doubt that if that figure were reduced by 2000 an important contribution would have been made to the bed problem throughout the region?

I suggest that the problem need not be such a long-term one as is generally supposed. A year ago the Cornwall County Council appointed a geriatrician to this area which included seven public-assistance institutions and 450 aged sick patients. No special facilities were available and no accommodation for these patients at any general hospital. An active unit was, however, established at one of the best of the public-assistance institutions in the area and specialist services made available. Coöperation by the profession and the nursing and voluntary bodies has already resulted in an appreciable number of these patients being sent home. More could go if they had homes to go to or if a suitable hostel were available.

Here, however, is the rub. A progressive local authority in association with public-spirited local people is about to open a hostel, but nobody has statutory power to coördinate the service it provides with that of the geriatric unit. Coöperation may be established on a voluntary basis as has already been done in the area by the establishment of an advisory committee between management committee and local authority to cope with the problems presented in "joint user" hospitals. If, however, such a committee is not given statutory power difficulties are sure to arise, particularly as the service for the chronic sick increases in scope.

To conclude I make the following suggestions which I believe would materially further a solution:

1. That the Government should take active steps to encourage the training of junior specialists at established geriatric units. At present it is extremely difficult to get suitable applicants to fill junior posts at some of these hospitals.
2. That first priority should be given to the requirements of these units so far as building and equipment are concerned. It is exasperating to find that the work at some of them is being delayed by lack of the most elementary necessities.
3. That a clause be introduced in the amending Act shortly to be brought before Parliament, giving statutory power to a joint committee of regional hospital boards, local authorities, and interested voluntary bodies to supervise the developing geriatric service.

The time for action is now while the service is still young.

Truro. C. T. ANDREWS.

SIR,—The letter of Dec. 25 from the secretary of the Emergency Bed Service, in which he shows that applications for hospital admission have risen by some 300–400% since the appointed day, contains the following:

> "The use of the Emergency Bed Service by doctors is purely optional; there is nothing to prevent a direct approach to the hospitals. In this respect the service was unaffected by the appointed day. Why then did the number of applications increase so greatly on July 5? There can be no definite and simple answer to this question, but it seems probable that many hospitals decided that after the appointed day they would treat their nurses fairly and stop overcrowding."

May I point out that in my view there is a direct and simple answer to the question why applications for admission to the E.B.S. have so greatly increased? Before the appointed day the vast majority of applications for admission, especially of patients not readily acceptable, were made to the local authorities, and in particular to the London and Middlesex County Councils, who, in common with the other local authorities, were statutorily

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obliged to provide accommodation for the sick, both acute and chronic. These applications came not only from general practitioners but quite commonly from other hospitals, especially teaching hospitals. Nowadays, so far as one can gather, there is no legal obligation on anybody to provide hospital accommodation for the sick; nor is any particular hospital, or group of hospitals, compelled to provide accommodation. Therefore the resort to the putting up of extra beds would seem to be on the decline and, as Mr. Peers has pointed out, many hospitals formerly compelled to this extremity have decided that "they would treat their nurses fairly and stop overcrowding." That the rate of applications will rise within the next three months is virtually certain, in which case his prognostication that "a very serious situation will arise" seems unhappily only too likely to be fulfilled.

The Medical Press, London, W.C.2. G. E. BREEN.

A REGISTRARS' GROUP

SIR,—We are much interested to know that a Registrars' Group has been formed in the Liverpool region (Dec. 4, p. 908). There has been a similar organisation in Birmingham since the beginning of the National Health Service, and the writers of this letter are a small sub-committee elected to study the problems of the registrar class in relation to the service.

Our interim regional consultants and specialists committee readily agreed to a request for one of our members to serve on their committee, and we are now able to send an observer, who has at present no powers of voting but is able to take part in the discussions. This enables us to keep in touch with the revolutionary changes taking place in medicine today, as well as to represent our own interests when necessary. It is anticipated that one or two registrars will be given full membership in the permanent consultants and specialists committee, and arrangements are being made to hold, early in the New Year, a further meeting, representative of the whole West Midland region, with the object of selecting two nominees to serve on the committee.

It is important that the potential specialists of the National Health Service should take part in discussions which so greatly affect them. Also, by the nature of their work, they are in the closest touch with the general running of the hospital, besides having a particular interest in certain administrative details such as medical records, forms, and the follow-up of patients. In many such matters they could give valuable help.

A. B. BLACK
C. F. HAWKINS
P. H. DAVISON
B. H. PRICE.

Birmingham.

HOSPITAL BIOCHEMISTS

SIR,—The points I raised in my letter of Dec. 4 have been answered to some extent by your correspondent "Clinical Biochemist" (Dec. 18). I think we are both agreed that the best person for the post of hospital biochemist is a chemical graduate with a medical degree; we differ when we have to choose between a non-medical chemist (N.M.C.) and a non-chemical medical man (N.C.M.). The points at issue are then: which is the better choice, and should they receive different salaries?

Let us consider the advantage of one over the other. (1) An N.C.M. can act as medical consultant whereas an N.M.C. cannot do so. (2) An N.M.C. is a better chemist than an N.C.M. (I sincerely hope that "Clinical Biochemist" will concede this point). In these days of hormones and vitamins I maintain that this is of more importance than (1) and is likely to become still more so in the future.

If a higher salary is paid to an N.C.M. than to an N.M.C. it should be paid only if he has had a longer training and for no other reason. The relevant training of an N.C.M. is 5–6 years for his degree and 1 year on the house, followed by, say, 2 years doing biochemistry; that of N.M.C. (considered as a PH.D.) is 5–6 years depending on the university, followed by, again say, 2 years specialising in hospital biochemistry. It would appear, therefore, that the N.C.M., having spent one year longer in training than the N.M.C., should be paid at a slightly higher rate (about £50 per annum higher, not £500).

After commenting on my previous letter "Clinical Biochemist" rashly proceeds, on the basis of his own experience, to belittle the capabilities of non-medical biochemists in general. He has even formulated a rule about the science graduate—namely, that he cannot hope to be more than a high-grade technician as far as his medical colleagues are concerned. This rule is apparently proved to his satisfaction by the fact that one chemist (non-medical) has been appointed to a chair of chemical pathology. PH.D.

PRESCRIPTIONS FOR PRIVATE PATIENTS

SIR,—In your issue of Dec. 25 Mr. Bevan, in replying to a question concerning the prescription of drugs to private patients, is reported to have said: "I am not prepared to allow public money to be spent on any form of activity where we shall not have the power to correct abuses."

To me it seems tragic rather than laughable that a man who has—if the report is correct—so little grasp of elementary logic should be at the head of one of the greatest spending departments of the Government. For those same doctors who may not prescribe a sixpenny box of pills for their private patients at the expense of the National Health Service may nevertheless keep such a patient off work and "on the box" for almost indefinite periods of time on their own sole responsibility—a vastly more expensive "form of activity," where the Minister does not, so far as I am aware, "have the power to correct abuses."

Stafford. JOHN FREW.

ŒSTROGENS AND DIABETES

SIR,—In an annotation on Oct. 23 the possibility of using œstrogens as an adjunct to, or substitute for, insulin in the treatment of diabetes mellitus was discussed. It might be thought that the benefit which accrues to mother and fœtus when a pregnant diabetic is treated with œstrogen and progesterone along the lines advised by White and Hunt,[1] might be due to an antidiabetic action of the hormones. That this is probably not so is shown by the case of a diabetic, 20 weeks pregnant, who was satisfactorily standardised with 14 units of insulin morning and evening. This patient had been receiving 40 mg. stilbœstrol and 20 mg. progesterone daily for 3 weeks. These hormones were then withheld for 2 weeks without any increase in the patient's insulin requirements.

In some cases of Simmonds's syndrome seen during the last three years œstrogens alone have been prescribed, and although these patients are liable to attacks of spontaneous hypoglycæmia no such attacks have been observed to be precipitated by œstrogen therapy. If, however, any hypoglycæmic action exerted by œstrogens is effected by depressing the secretion of diabeticogenic hormone by the anterior lobe of the pituitary, then this lack of reaction is to be expected in this syndrome where anterior-pituitary function is very severely damaged.

Liverpool. S. BENDER.

WEATHER AND ILLNESS

SIR,—Your annotation last week is of particular interest to me as I am trying by statistical methods to establish the relationship between atmospheric changes and the condition of sufferers from rheumatic diseases. I am looking closely into the matter of movements of pressure systems and fronts, and have devised for my own use a code which enables such conditions to be recorded concisely, permitting easy classification for statistical purposes.

In this inquiry I am seeking to get in touch with sufferers—preferably those able to carry on with their normal occupations—who are willing to keep a record of the severity of pain, and send me a note, about every three months, with dates and approximate times. It would be very helpful if doctors could put such patients in touch with me.

All correspondence is, of course, treated as strictly confidential, but there is no real necessity for me to be

1. White, P., Hunt, H. *J. Amer. med. Ass.* 1940, **115**, 2039.

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aware of the identity of observers so long as I have, at the doctor's discretion, details of domicile and movements for any considerable distance, and such general, non-technical, information on the case as will obviously be needed.

While I am quite aware of the many complications involved in such an inquiry, I am hoping, by establishing pronounced general trends, to furnish new data of value as a starting-point for further research.

9, Inveresk Gardens, Worcester Park, Surrey. A. J. WHITEN.

MULTIPLE-PRESSURE VACCINATION

SIR,—I was interested to read Dr. Rees's article of Dec. 11. In a recent investigation of the multiple-pressure method of vaccination on Service personnel, the following results were obtained.

Of 204 unselected adults, all of whom had been vaccinated by scarification 5–7 years before, there were 32 in whom vaccination had been unsuccessful—that is, three scarifications at weekly intervals had failed to produce vesiculation by the 7th day. These 32 were divided into two equal sections. Of 16 vaccinations by scarification 6 were successful, while of 16 by multiple pressure 11 were successful. The remaining 172 were also divided into two equal sections; one was vaccinated by scarification and the other by multiple pressure. The criterion of success was vesiculation in 2 to 7 days—an accelerated reaction being counted as successful. The results were as follows:

Method	No. of subjects	No. of takes	
		1st attempt	2nd attempt
Scarification	86	56	6
Multiple pressure ..	86	74	4

It was not possible to proceed further owing to movement of personnel, but the results show the superiority of multiple pressure over scarification both in those who have been previously vaccinated successfully and also where previous scarifications have been unsuccessful and the subjects have been labelled "immune" or "insusceptible."

London, S.W.3. M. C. JOSEPH.

OSTEOPATHY

SIR,—As a medically qualified osteopath, I was pleased to read Mr. Batchelor and Mr. Cohen's article on their visit to the London College of Osteopathy. It was a fair and reasoned expression of opinion, gleaned from such a visit. It cannot, of course, be a fair and reasoned opinion following an extensive study of the subject, as they admit.

There are two points on which I would like to comment. I do not consider that surgeons of twenty years' standing should necessarily be able to appreciate the "fine variations" of position and mobility of a vertebral joint. One would not expect to be able to appreciate the fine variations of the female pelvic viscera upon doing a bimanual examination for the first time. No doubt general surgeons perform bimanual examinations innumerable times during twenty years, but surely the gynæcologist would be in a much better position to appreciate the fine variations of size and position of these structures. I consider this a fair analogy.

So too, I would like to counter the remark that "craftsmanship in manipulative therapy is not to be regarded as a major achievement." I agree, however, that "manipulative therapy is only a minor weapon in the medical armamentarium." These two statements are quite different. I would say, most categorically, that this craftsmanship is indeed a major achievement, for the practitioner concerned. Because it is difficult to achieve, there are but few who become really proficient in the art. Certainly the orthopædic surgeon who does two or three manipulations a week could never become skilled in the practice of manipulation, as the skilled osteopath does. Yehudi Menuhin may be able to play the piano, but he could never be a master of the piano as he is of the violin. Such is the art of manipulation that its perfection lies in constant and continuous practice. It must be a full-time occupation, not an occasional pastime. A thoracic surgeon may be able to perform an operation on the brain, but would he be really skilled in it?

It is this very fact that manipulation needs arduous application on the part of the devotee which has led to the waning of interest on the part of the orthopædic surgeon. No wonder the results are unsatisfactory and indifferent, while orthopædic surgeons use the blunderbuss methods that they are wont to use. What is the use of forcibly straining the whole vertebral column by means of manipulation under anæsthesia, when there is for example, merely a lesion of the lumbo-sacral joint? Where orthopædic surgeons fail is in their lack of precision in manipulating the joint of the spine in question. Where the osteopath succeeds is in the detailed examination of the movements of each vertebral joint, and of its position and the subsequent localised manipulation, which should be confined to the faulty joint alone. This precision of manipulation is the most difficult of all to acquire. Without adequate training and practice in the art of manipulation, none can hope to be really successful in this fascinating subject.

Incidentally, it is not easy for the medically qualified osteopath to obtain an opportunity to prove the value of the method in hospitals. I personally have been turned down for an appointment in the physiotherapy department of a London teaching hospital, merely because I had an osteopathic qualification, and in spite of the fact that none of the other candidates had equally good qualifications in a purely medical sense. I am glad to be able to say, however, that I was appointed later to a hospital with a less biased medical staff.

London, W.1. ALAN STODDARD.

SIR,—The Select Committee of the House of Lords on the Registration and Regulation of Osteopaths Bill, quoted in your leading article of Dec. 25, did not specify in its recommendations that osteopathic education should be confined to postgraduate medical colleges, which is the status of the London College of Osteopathy, but that it should be developed in one or more well-equipped and properly conducted institutions in Great Britain.

Furthermore, as you stated, the advice did not fall upon deaf ears. Long before 1946 and the inauguration of the L.C.O., the British School of Osteopathy was completely reorganised into a charitable, non-profit-making institution, with Lord Hankey as one of three trustees. The educational records of this establishment are open to anyone's inspection, and it is affirmed that they would bear more than favourable comparison with those of the L.C.O.

At the same time that the B.S.O. was reorganised, the General Council and Register of Osteopaths was instituted and undertook to lay down standards of osteopathic education. The gentlemen responsible for the inauguration of the L.C.O. gave their full coöperation in the establishment of these standards, with which the B.S.O. has since fully complied.

The London College of Osteopathy, on the other hand, has spurned these standards, substituting for them other standards, which have been condemned by the American Osteopathic Association. The British School of Osteopathy, having faithfully followed the advice of the 1935 Select Committee, has built itself up by persistent endeavour and has won public confidence. Its complement of students now is over thirty, whereas the L.C.O.'s six students have, to the best of my knowledge, dwindled to one.

A. W. ELLIS
Editor, *Osteopathic Quarterly.*

London, E.C.4.

SIR,—I agree with Mr. Charnley: let us be scientific. That is, let us not blink the facts. Anybody who has seriously investigated osteopathy, without being blinded by prejudice, must know that there are very many cases in which it works. Also that a large proportion are cases which represent a failure of orthodox methods. I myself have, in the last twenty-five years, seen—and

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often followed up—scores of cases which have been quickly and permanently relieved by a few treatments by osteopaths. I have, of course, seen failures too.

I personally am more interested in getting my patients well than in a-priori theorising. Hence, if I am satisfied that certain treatment is good, I will use it first and enter into discussion as to how it works only as a secondary consideration. I suggest that if more surgeons were to study the thing at first hand, this would be the most effective way of doing away with both "unqualified" practice of osteopathy (the American graduate has a four-year training!) and with the accusation so often brought—and not altogether without justification: see Mr. Charnley's letter—that the profession is hide-bound.

London, S.W.3. L. J. BENDIT.

POSTOPERATIVE PERIOD

SIR,—Your leading article last week is fairly and lucidly written, but I doubt if the majority of doctors will agree with your conclusions. My experience as a general practitioner and part-time specialist is that most doctors are disgruntled and most patients under the N.H.S. are no better off but rather worse off.

London, N.W.11. L. S. WOOLF.

NURSING EXPERIENCE FOR MEDICAL STUDENTS

SIR,—In our hospital a scheme will shortly be introduced whereby students will give up three weeks of their course to do general nursing tasks under the supervision of ward sisters. Whilst it cannot be denied that some knowledge of ward routine would be gleaned we feel strongly that such expenditure of time is ridiculous in an already overcrowded curriculum. In two years as a clinical clerk and dresser the student cannot help becoming sufficiently acquainted with this routine.

Lest it should appear that we are embittered by such domestic duties, we wish to point out that we are now in our final year and are unaffected by the change.

Would it not be better if we had the opportunity of performing but one forceps delivery? We write in the hope that such a scheme may not spread to other hospitals.

London Hospital Medical College, London, E.1. R. H. CARRUTHERS R. E. RICHARDSON.

PROFESSIONAL SECRECY

SIR,—You have taken an interest in sustaining the profession in its struggle against Ministerial compulsion to disclose professional secrets. It is encouraging to find that the Minister of Health has been constrained to annul by regulation (no. 2517, 1948) the repeal of the Act of 1916 which made it a statutory obligation to ensure to patients suffering from V.D. complete confidentiality of records of their disease.

I have a special interest in this matter. In April, 1928, the Edinburgh Corporation was promoting a Bill in Parliament, imposing notification of venereal disease in their area. Mr. Pethick Lawrence (as he then was) moved, and I seconded, a motion for rejecting the Bill, which was strenuously supported by the Scottish Department and Scottish members. The motion was approved by a large majority, and patients suffering from V.D. enjoyed statutory protection against the disclosure of their condition, until the N.H.S. Act, 1946, automatically removed that protection.

Mr. Bevan's retreat has been occasioned, not by medical, but by lay, pressure, the spearhead of which has been the Association for Moral and Social Hygiene. It is encouraging to learn that the bodies which have won this victory are becoming interested in the opposition to Statutory Instruments 506 and 507, which must widen the area in which disclosure must be made of the medical records of patients treated under the N.H.S. Act, 1946.

It is still more encouraging that the Fellowship for Freedom in Medicine is issuing as one of its earliest bulletins to the public a strong protest against the extending compulsion on doctors to place their medical records of State patients at the disposal of various lay bodies, thus necessitating breaking the Hippocratic oath, which has governed the conduct of the medical profession in all civilised countries from immemorial ages. It is adding to this protest the demand that the Amending Act shall assure the withdrawal of these regulations.

House of Commons. E. GRAHAM-LITTLE.

ILLUSIONS WHILE FALLING ASLEEP

SIR,—The phenomenon described by Dr. Nettell (Dec. 18) is not uncommon, both in psychoneurotics and in people not labelled explicitly as such. Like other unpleasant dreams occurring repeatedly in the same form, it is at times a rather troublesome experience. We may assume that Dr. Nettell's patients have also had other disorders, very likely of the psychosomatic type in the narrower sense of the word. In such instances the disturbance of self-perception—even though only during superficial sleep—must be considered as part of the syndrome from which the patient happens to suffer. The condition of superficial sleep conduces to the experience of disintegrated perception of the somatic self; the dominant content of hypnagogic hallucinations is frequently the position of one limb or the irritation of an organ-function, pictorially expressed.

May I advise that no practitioner attempts to interpret analytically the phenomena of enlarged head or limb, &c., to his patient? The risks are the stimulation of further unpleasant sensations and hypochondriac obsessions. He should, however, explain that the phenomena in question are insignificant and only part of people's occasional general "nervousness." If it is decided to discuss the patient's life situation and stresses, this should be done manifestly with a view to improving the other, psychosomatic, complaints; and the hope should be expressed that the hypnagogic phenomenon may also cease with time. To hasten the transition between half sleep and deep sleep, sedatives with cortical and subcortical actions (e.g., bromide gr. 15 with sod. barbitone gr. 7½) may be useful in cases of recent origin; though patients of the introspective and obsessional type may not react well to this therapy.

Patients who complain of these symptoms while being treated for psychoneurosis are almost always personalities of the autistic make-up and are suffering from rather deep-seated deficiencies and severe symptoms. In a number of such cases I could not avoid the impression that the experience of inflated head or limb was indeed a distorted hallucinatory picture of genital erection; this may be true, of course, in females as well as males. This is one of the reasons for my warning against any symbolic interpretation of it outside a carefully handled psycho-analytical situation.

Department of Psychological Medicine, St. Bartholomew's Hospital, London. SAMUEL LOWY Clinical Assistant.

STAPHYLOCOCCAL COAGULASE

SIR,—In many articles in the *Lancet* and other journals and in textbooks one often finds statements about the staphylococcal coagulase (e.g., Moss et al. *Lancet*, 1948, i, 320). In English and American literature the circumstances of the discovery of this enzyme are, however, nearly always omitted or wrongly given. Though Much [1] was the first to observe the coagulating activity of staphylococci on fibrinogen, he did not recognise the importance of this property in relation to virulence. This is why in the two decades after his finding no further work had been done on this subject.

In 1926 I found [2]—without knowing about Much's previous experiments—that the fibrinogen-coagulating property was confined to virulent staphylococci. My work established this as a valuable method of differentiating pathogenic from non-pathogenic staphylococci. The finding of this differentiation was more important than the observation that some cocci possessed a coagu-

1. Much, H. *Biochem. Ztschr.* 1908, **14**, 143.
2. *Zbl. Bakt.* 1926, **99**, 74. *Wien. med. Wschr.* 1927, **77**, 149.

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lating property; for staphylococci are ubiquitous, and harmless skin staphylococci can easily contaminate a blood-culture or can complicate diagnosis because of their presence in the intestine and elsewhere.

It was not until after my paper appeared in 1926 that others began to work on the coagulase, fully acknowledging my discovery (e.g., Gross and Neisser in 1927). Later many methods were described for estimating coagulase production, but mostly without mentioning my original finding and method. I am convinced also that the original method which I described in 1926 gives the most decisive results; in this the citrated blood is wholly coagulated, and a positive result is obtained only with definitely pathogenic staphylococci. I work with agar cultures and with 1% citrated blood. The procedure is the simplest of all methods.

I hope that in future my contribution to our knowledge of the staphylococcal coagulase will not be forgotten in English and American publications.

University of Budapest. J. DE DARÁNYI.

*** Much showed that all strains of *Staphylococcus aureus* were coagulase-positive, whereas other types of staphylococcus, such as *albus* and *citreus*, and all other micro-organisms were coagulase-negative. He remarked that all his positive strains were of "human pathogenic origin." It would seem, therefore, that Much deserves the credit for first demonstrating this association, even though Professor de Darányi and others later made the same discovery independently.—ED. L.

Obituary

REGINALD HENRY MILLER

M.D. LOND., F.R.C.P.

Dr. Reginald Miller, consulting physician to St. Mary's Hospital and Paddington Green Children's Hospital, died in London on Dec. 23, at the age of 69.

The son of Dr. Andrew Miller, of Hampstead, he was educated at Charterhouse and St. Mary's Hospital, qualifying M.B., with distinction in medicine, in 1905. Soon afterwards he became house-physician at St. Mary's to Dr. D. B. Lees, who fostered his interest in children's diseases and especially acute rheumatism. From 1906 to 1908 he was registrar and pathologist at the Hospital for Sick Children, Great Ormond Street, and he was elected to the staff of St. Mary's in 1910.

That he had a graceful and fluent pen was early evident from his editorship of the *St. Mary's Gazette*. Later, with his friend Hugh Thursfield, he edited the *Archives of Diseases in Childhood* from the journal's inauguration in 1926 until 1933 when it was well established; and he also edited the pædiatric section of the *Medical Annual*. His own investigations, reflected in his writings, were mainly into cœliac disease, the digestive disorders of childhood, and rheumatic fever and its cardiac complications; at Paddington Green he organised the first supervisory rheumatic clinic for children in London, and he was an original member of the British Pædiatric Association. He was also visitor for the county of Middlesex under the Mental Deficiency Acts. In 1936–37 he was a councillor of the Royal College of Physicians. In 1939 he became physician in the E.M.S. at Park Prewett Hospital, Basingstoke, and he was afterwards director of the medical division until the hospital was disbanded.

"Reginald Miller," writes C. A. P., "understood the mentality of children, even the youngest, and quickly gained their confidence; so it is not surprising that he excelled in the management of their illnesses. With his six feet two or so he must have seemed a prodigious height to the tiny creatures who so immediately became affable with him. Brought up to rely upon clinical acumen and the information obtained by percussion and auscultation, he sometimes seemed indifferent to the aids of the modern laboratory. In reality he showed great discernment in what he accepted and what he thrust from him as scientifically pretentious, voicing his opinion in biting sarcasm or a witty aphorism. In debate his remarks were often permeated with subtle humour; he could sum up a situation in a phrase and destroy an opponent's case by kindly ridicule. At Park Prewett he was extremely loyal to his registrars and residents, and he worked hard for the betterment of the conditions, not only of them, but of the nursing staff of the improvised hospital in which he found himself."

"To colleagues and students alike," adds F. L., "he was an accepted wit, with a sparkling vein of humour, which, though often trenchant, was never wounding, and in teaching was constantly used to gild the philosophic pill. The maintenance of the honour, dignity, and ethical standard of the profession meant much to him."

K. H. T. writes: "Miller was a very able clinician, being essentially a practical physician of the older school: and he made significant contributions to pædiatrics, in which his main interest lay. His book on the *Medical Diseases of Children*, published in 1911, gave a really first-class account of this subject, and held its own for many years. He had a very ready wit, and would frequently enliven a hospital staff meeting by some caustic remark which was both penetrating and highly amusing but never malicious. His many friends and colleagues will always enjoy the memory of his massive frame and deep voice, and the great good humour which were so characteristic of him."

Dr. Miller was twice married. His second marriage was to Dr. Dorothy Gilford, who survives him. A devout Roman Catholic, he gave much of his time and thought to his family, with whom his life was notably happy.

WILLIAM SUSMAN

B.A., M.D. QUEEN'S UNIV., ONTARIO

Dr. Susman, who died on Dec. 23 at the age of 53, had been a member of the staff of the department of pathology in the University of Manchester since 1925, and for over twenty years a lecturer in morbid anatomy and histology.

From 1915 to 1919 he served with the Canadian Army Medical Corps, in the 8th and 2nd Duke of Wellington's Regiment, and in the Royal Flying Corps; he was twice wounded and was left with some permanent damage in one foot. After the war he studied medicine at the Queen's University, Kingston, Ontario, and he took his degree in 1923. His interest in pathology developed early, and after qualifying he spent two years in Edinburgh, with a Hoffmann fellowship, under Lorrain Smith, holding various pathological appointments in the university, the Royal Infirmary, and the Royal Mental Hospital there.

In 1925 he was appointed to an assistant lectureship in the department of pathology at Manchester under Shaw Dunn. He remained in the department, and for many years he had been the senior member of the staff. He was also senior pathologist to the Manchester Royal Infirmary and honorary pathologist to the Manchester Royal Eye Hospital at the time of his death. These appointments entailed a great deal of routine pathology and teaching, but he found time for much research and he published some 25 papers. His appointment to the Manchester Royal Eye Hospital gave him opportunities for studying a large amount of material, and his paper on the classification of intra-ocular tumours (1938) was an outstanding contribution to the subject. He was also interested in diseases of the endocrine glands, and his best-known paper on this subject described adrenal atrophy in Addison's disease (1932).

S. L. B., to whom we are indebted for much of this memoir, writes: "Dr. Susman was an experienced and forceful teacher of morbid anatomy and histology. He had a clear understanding of the needs and difficulties of the medical student, and he was particularly helpful to those in the elementary stages of the course. He always had the students' welfare at heart and he will be gratefully and affectionately remembered by many of them. A hard and conscientious worker, he readily placed his wide experience in pathology at the service of his colleagues and others to whom he acted as an unofficial consultant."

Dr. Susman leaves a widow and one son.

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Notes and News

EMBRYOLOGY OF THE MICROSCOPE

Dr. Ashworth Underwood and his colleagues at the Wellcome Historical Medical Museum (now at 28, Portman Square, London, W.1) have arranged a fascinating exhibition, with selections from the museum's collection of over 1000 microscopes, to explain how this instrument has developed since 1590, when the compound microscope was invented by Janssen, a Dutch maker of spectacles. Examples are given of the instruments, work, and writings of the chief microscopists, including Leeuwenhoek, Buffon, Swammerdam, Hooke, Malpighi, and Nehemiah Grew. The exhibits are planned to emphasise the chief steps, such as Hertel's (1716) plane mirror for reflecting light on to the specimen under examination, Culpeper's (1725) first concave reflecting mirror, the introduction of mechanical stages (1752), and Lieberkühn's concave silver mirror for viewing opaque objects and his projection microscope for use with the sun as the source of illumination, followed by Adams's projection microscope designed for an artificial source of illumination (the father of the magic lantern, epidiascope, and cinema projector). In the second half of the 18th century the clumsy contraptions of wood and cardboard, and the beautifully turned and decorated box microscopes, like the one made for Pope Benedict XIV (1750), were superseded by brass. Further development was held up until the invention of the achromatic lens (1826) by J. J. Lister, Lord Lister's father. This enabled mechanical improvements to appear, mainly to provide stability, leading to Ross's monstrosity that can only just be lifted by one person, and to the one of which Myall, in 1888, wrote: "We have here an elaboration of mechanical movements and illuminating arrangements the complexity of which almost defies comprehension." Refinements and adjuncts led to Ahrens's microscope for three observers, and another with candlestick attached for providing artificial illumination. The exhibition also contains examples of the earliest slides, with some of the original specimens mounted thereon, and a "flea microscope," in which a flea was permanently mounted in the instrument.

The exhibition is open, for a limited period, from 10 A.M. to 5 P.M. every day except Sunday. In other rooms the visitor may see an admirable exhibition illustrating the history of surgery.

RELEASE OF DOCTORS FROM SERVICES

THE Central Medical War Committee have been informed that the release of medical officers during the coming months will be as follows:

R.A.M.C.—Medical officers, including specialists: Group 73, Jan. 1–Feb. 9; Group 101, Feb. 10–17; Group 102, Feb. 18–26; Group 103, Feb. 27–March 5; Group 104, March 6–18; Group 105, starting on March 19.

R.A.F.—Medical officers, including specialists: Group 72, January; Group 73, February; Group 74, February.

AN INDEX OF NEW PRODUCTS

MANY find it far from easy to keep track of the numerous new pharmaceutical substances and preparations which come on to the market each year. This difficulty should, however, be mitigated by a new service which is being introduced by the *Pharmaceutical Journal*. Subscribers to this service will receive periodically a series of cards, each setting out information about a new substance, including details of composition, properties, indications, dosage, references to the literature, packing and price, and suppliers. The annual subscription of 2 guineas is payable to the *Pharmaceutical Journal* and should be sent to the journal (Dept. N.P.) at 33, Bedford Place, London, W.C.1. The first issue will consist of 70 cards (representing preparations introduced during 1948), a filing drawer, and guide cards. Subsequently additions will be made as new products appear.

LATENT TROPICAL DISEASE

THE Ministry of Health points out that there are now many people in this country who, through former residence in tropical or subtropical regions, have become infected with tropical diseases, the most insidious being amœbiasis, hookworm infection, and malaria. Those who are suffering from one or more of these infections in a chronic form may show no sign or symptom apart from a lowering of their general health just sufficient to impair enterprise and working capacity. Their condition may then be overlooked until some special circumstances cause the latent infection to flare up—chronic amœbiasis, or malaria, suddenly manifesting itself in acute form as a complication of surgical treatment is notorious. When a patient complains of vague and indefinite malaise and of lack of energy and initiative, previous residence in tropical or subtropical regions should therefore be inquired for. The diagnosis of the three conditions mentioned requires laboratory investigation, preferably at centres specialising in this kind of work, but the time and trouble involved will be justified by the reduction in chronic ill health and in surgical complications

SPLENECTOMY IN THREE GENERATIONS

Dr. Richard Harper, of Barnstaple, Devon, writes:

The photograph shows three generations of a family, with ability above the average, who owe their good health to

splenectomy, performed in each case for the relief of proven acholuric family jaundice.

Mr. Bertram S., aged 80, is active and well since splenectomy was performed in October, 1925, by Mr. J. E. Adams at St. Thomas's Hospital.

Winnie, his daughter, aged 30, was 14 when her spleen was removed at St. Thomas's Hospital by Mr. C. A. R. Nitch. She is now fit and strong.

Colin, her son, aged 4, had his spleen removed in December, 1946, at the age of 2 years 4 months, by Mr. A. L. Kenyon, at the Royal Manchester Hospital for Children.

PAY FOR HOSPITAL DOMESTIC STAFF

EARLY in December the ancillary staffs council of the Whitley Council for the health services agreed on revised rates of pay for domestic and manual workers in hospitals and institutions, and these will also apply to such workers in residential institutions controlled by local authorities. It is noteworthy that the new rates are to apply throughout Great Britain—a plan which has never been attempted before—with the result that urban and rural rates will be paid outside the London area, instead of those decided locally, in the past, by the provincial councils of the former National Joint Council for Staffs of Hospitals, and the former Scottish National Joint Committee for Domestic Staffs in Hospitals. Moreover, all hospitals, including mental hospitals, will offer the same rates.

For basic grades the new rates are 100*s.* for men and 75*s.* for women in urban areas, and 97*s.* for men and 74*s.* for women in rural areas. In London the rates will be 106*s.* for men and 82*s.* for women. These new basic rates will in general mean a rise of 1–8*s.* a week for men and 2–7*s.* a week for women, and they are based on a 48-hour week. In all some 130,000 people are affected. In a few hospitals staffs have been receiving higher rates than these, and will be allowed to retain them on a personal basis. The increases date from the beginning of the pay week which included Nov. 1, 1948.

Association of Whole-time Salaried Specialists

A meeting open to all whole-time salaried specialists, whether members of the association or not, to discuss matters of common interest, particularly in connexion with the National Health Service, will be held at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, on Friday, Jan. 28, at 4 P.M. Dr. Horace Joules, the president of the association, will be in the chair.

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University of London

At recent examinations the following candidates were successful:

M.S. (Branch I, Surgery).—D. T. A. Brown, S. I. Green, H. O. Jones, D. W. Williams.

Dr. C. Keith Simpson has been appointed part-time reader in forensic medicine at Guy's Hospital medical school. Mr. C. B. Allsopp, PH.D., has been appointed reader in physics at the school.

The title of reader in applied pharmacology has been conferred on Dr. Andrew Wilson, in respect of the post he holds at University College and University College Hospital medical school.

National Association of Home Help Organisers

A meeting of the association will be held on Saturday, Jan. 22, at 2.30 P.M., in Westminster City Hall, Charing Cross Road, London, W.C.2, when Sir Wilson Jameson will speak on the Future of the Home Help Service.

Institute for the Scientific Treatment of Delinquency

Six lectures on Difficult and Delinquent Personalities: the Freudian Approach will be given at the institute by Miss Barbara Low, on Feb. 22, March 8, 15, 22, 29, and April 5 at 6 P.M. Application for tickets should be made to the education secretary of the institute, 8, Bourdon Street, London, W.1.

Dr. Desmond Curran has been appointed a member of the committee appointed by the Home Secretary to review prison methods of punishment. The chairman is Mr. H. W. F. Franklin, headmaster of Epsom College.

Appointments

ASLETT, E. A., M.R.C.S., D.T.M. & H.: chest physician, Merthyr and Aberdare area.
BROWNE, J. C. M., M.B., B.SC. Lond., F.R.C.S.E., M.R.C.O.G.: asst. lecturer in obstetrics and gynæcology, Postgraduate Medical School, London.
COHEN, H. M., M.D. Lpool, D.P.H.: school M.O., Birmingham.
COX, J. G., M.R.C.S.: chest physician, Pontypridd and Rhondda area.
CRAMOND, JAMES, M.B. Aberd., D.P.H.: deputy M.O.H., Tottenham.
FRASER, JOHN, M.B. Aberd.: medical superintendent, Astley Ainslie Hospital Convalescent Hospital group.
GIBSON, ANNE, M.D. Edin.: pathologist, South London Hospital for Women and Children.
GREIG, J. C. R., M.B. Edin., F.R.C.P.E.: physician, Outer Hebrides area.
HOLDEN, EDWARD, M.R.C.S., D.A.: specialist anæsthetist, West Cumberland Hospitals.
HOPPER, MADGE, M.B., B.HY. Durh., D.P.H.: area executive M.O., South area, Northumberland, and M.O.H., Gosforth.
JOYCE, J. B., M.R.C.S., M.R.C.O.G.: asst. obstetrician and gynæcologist, Workington Infirmary.
MACPHERSON, A. D. H., M.B. St. And.: bacteriologist, Northern Regional Hospital Board.
PEARCE, J. D. W., M.A., M.D. Edin., F.R.C.P.E., D.P.M.: asst. physician, department of psychiatry, St. Mary's Hospital, London.
ROBB, T. M., M.R.C.S., D.M.R.T.: director, radiotherapy department, Lambeth Hospital.
THOMSON, I. S. D., M.B. Edin., F.R.C.S.: asst. E.N.T. surgeon, Aberdeen General and Special Hospitals.
VOSS, H. J., M.R.C.S.: pathologist, Kettering General Hospital, and associate pathologist, Northampton General Hospital.
WYPER, J. F. B., M.B., B.SC. Glasg., M.R.C.O.G.: asst. obstetrician and gynæcologist, Aberdeen General and Special Hospitals.

Colonial Service:

BEADNELL, H. M. S. G., M.R.C.S.: asst. superintendent, Mental Hospital, Barbados.
BOYD, P. I., M.D. Lond., D.P.H.: M.O.H., Leeward Islands.
BURY, E. J., M.R.C.S., D.T.M. & H.: senior health officer, Nigeria.
COOK, JAMES, L.R.C.P.E., F.R.C.S.E.: surgical specialist, Hong Kong.
COOKE, R. O., M.D. Dalhousie: senior M.O., Mental Hospital, Jamaica.
HAGEN, J. M., M.B. Edin.: house-surgeon, Federation of Malaya.
HENNESSEY, R. S. F., M.D. Dubl., M.R.C.P.I., D.T.M. & H.: deputy director of medical services, Uganda.
HUDD, H. R., M.B. Wales: M.O., Uganda.
JONES, C. R., M.B., B.SC. Wales: M.O., British Guiana.
MCLAGAN, FRANCIS, M.B. St. And., M.R.C.P., D.P.M., D.T.M. & H.: director of medical services, Sierra Leone.
MACLEAN, D. J. A., M.B. Edin.: M.O., Nyassaland.
MANUWA, S. L. A., M.D. Edin., F.R.C.S.E., D.T.M. & H.: regional deputy director of medical services, Nigeria.
MERRETT, W. E. S., O.B.E., B.M. Oxfd: principal, medical school, Nigeria.
MURRAY, DOUGLAS, M.B. St. And., D.P.H.: regional deputy director of medical services, Nigeria.
PEARSON, F. A., B.SC. Lond., M.R.C.S.: temporary M.O., Nigeria.
PERKINS, J. D. B., L.M.S.S.A.: M.O., Tanganyika.
ROYES, K. C., M.A., B.M. Oxfd, D.P.M.: M.O., Mental Hospital, Jamaica.
SMITH, C. E. G., M.B. St. And.: M.O., Federation of Malaya.
WYNTER, L. R., M.D. Dalhousie, D.O.M.S.: ophthalmic surgeon and asst. medical superintendent, Leeward Islands.

Diary of the Week

JAN. 9 TO 15

Monday, 10th

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
8.30 P.M. Mr. W. Grant Waugh, Mr. W. A. Law: Treatment of Osteo-arthritis of the Hip and Knee.
WESTMINSTER HOSPITAL MEDICAL SCHOOL, Horseferry Road, S.W.1
5.30 P.M. Clinico-pathological demonstration on Cancer of the Pharynx.

Tuesday, 11th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. C. J. Gavey: Cardiology of Old Age. (First Goulstonian lecture.)
INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: Histopathology of the Skin
CHELSEA CLINICAL SOCIETY
7.30 P.M. (South Kensington Hotel, 47, Queen's Gate Terrace, S.W.7.) Prof. D. W. Smithers, Prof. W. V. Mayneord, D.SC.: Radio-active Isotopes in Treatment.

Wednesday, 12th

ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St. Vincent Street, Glasgow
5 P.M. Dr. H. C. Cameron: Beginnings of Modern Surgery with personal recollections of Lord Lister. (John Burns lecture.)

Thursday, 13th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. Gavey: Cardiology of Old Age. (Last Goulstonian lecture.)
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, S.W.1
4.30 P.M. Neurology lecture-demonstration.
INSTITUTE OF DERMATOLOGY
5 P.M. Dr. H. W. Barber: Influence of Stress in Dermatology.

Friday, 14th

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. N. Lloyd Rusby: Application of Collapse Therapy in Pulmonary Tuberculosis.
MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, W.9
5 P.M. Prof. S. Nevin: Case demonstration.

Births, Marriages, and Deaths

BIRTHS

RUTCHER.—On Dec. 23, the wife of Dr. H. G. Butcher—a daughter.
FISHER.—On Dec. 29, in London, the wife of Dr. R. E. W. Fisher—a daughter.
GORDON.—On Dec. 25, the wife of Dr. I. R. S. Gordon—a son.
KNIGHT.—On Dec. 26, in London, the wife of Mr. G. C. Knight, F.R.C.S.—a son.
ORMISTON.—On Dec. 25, at Winchester, the wife of Dr. George Ormiston—a son.
PASSMORE.—On Dec. 20, in Edinburgh, the wife of Dr. R. Passmore—a son.
WARD.—On Dec. 27, at Cheddar, the wife of Dr. A. J. Ward—a son.
WILKIE.—On Dec. 28, the wife of Dr. Duncan Wilkie—a son.

MARRIAGES

HABIBIS—MURRAY.—On Dec. 29, in London, Homer A. Habibis, M.D., to Stella Mary Murray, M.B.
SILVER—CUFFE.—On Dec. 29, at Winchester, Peter Silver, M.B., to Patricia Anne Cuffe.
YOUNG—CLARKE.—On Dec. 22, in London, Francis L. D. Young, M.R.C.S., to Barbara Lucy Clarke.

DEATHS

ALDRIDGE.—On Dec. 26, at Bournemouth, Charles Braxton Mooring Aldridge, M.A. Camb. M.R.C.S., aged 71.
BALTHASAR.—On Dec. 29, in London, Ewald Mouat Balthasar, M.R.C.S., D.P.H., aged 66.
DOCKRAY.—On Dec. 29, John Vernon Dockray, O.B.E., M.A. Camb., M.R.C.S.
GARRAD.—On Dec. 26, Francis William Garrad, B.A., M.D. Camb., aged 78.
HOLLWAY.—On Dec. 26, at Teignmouth, Edith Blake Hollway, O.B.E., M.B. Lond.
HUTCHINSON.—On Dec. 25, at Worthing, Richard Cecil Hutchinson, M.D. Manc., D.P.H.
LANE.—On Jan. 2, in London, Clayton Arbuthnot Lane, M.D. Lond., lieut.-colonel I.M.S. retd, aged 80.
MACKAY.—On Dec. 28, at Cheltenham, James Murdoch Mackay, M.C., M.B. Glasg.
MILLER.—On Dec. 23, in London, Reginald Henry Miller, M.D. Lond., F.R.C.P.
MOSSMAN.—On Dec. 24, at Baledmund, Pitlochry, Robert Arthur Mossman, L.R.C.P.E., aged 94.
PASSMORE.—On Dec. 31, William Henry Passmore, M.R.C.S., aged 76.
PHILLIPS.—On Dec. 25, at Bwlch Glas, Nevin, North Wales, George Phillips, M.D. Edin., aged 79.
RAW.—On Dec. 26, Stanley Raw, M.D. Durh., F.R.C.S.
SUSMAN.—On Dec. 23, at Didsbury, Manchester, William Susman, B.A., M.D. Ontario, aged 53.
WILSON.—On Dec. 28, at Teddington, Middlesex, Graham Lionel John Wilson, M.A. Oxfd. M.R.C.S., aged 84.
YOUNG.—On Dec. 28, at Bedford, William John Young, M.R.C.S., aged 79.

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HISTORICAL BUILDING
DES MOINES, IOWA

LATE SOCIAL RESULTS OF PREFRONTAL LEUCOTOMY

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PHYSICIAN SUPERINTENDENT

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RUNWELL HOSPITAL, ESSEX

PREFRONTAL leucotomy is now widely used, and in some quarters is becoming a routine treatment. Ten years have passed since the early cases were operated on, and we should begin to know the total and permanent effects. There is much impressive evidence of the disappearance of presenting mental symptoms, but less information about the lasting defects produced in the person as a whole. We give here some data about the social adaptation of leucotomised patients relative to the disappearance of their psychiatric symptoms.

According to Freeman and Watts (1948):

> "It is becoming more and more plain that patients who undergo lobotomy must sacrifice some of the virtues, some of the driving force, uplift, altruism, creative spirit, soul, or whatever else one would like to call it. The more the patient is endowed with this in the first place, the better the eventual outcome."

With the first part of this statement we certainly agree. We go much further than this, however, and say that qualities much less subtle and spiritual than that referred to are, as a rule rather than as an exception, destroyed by the operation. In fact, by considering the very practical issues of work, pleasure, and social status, together with the presence of severe antisocial features, it can be shown that the psychiatric recovery is often gained at the expense of great reductions of the efficiency, enjoyment, and acceptability of the person. These conclusions lead to a disagreement with the second part of Freeman and Watts's statement. The more the patient is endowed in the first place with this spiritual quality, or for that matter with any higher quality, the worse is the relative outcome in the end, for that particular patient.

METHOD OF STUDY

No doubt one of the reasons for delayed realisation of the extent of the damage to the personality has been a failure to examine all aspects of the results. Our aim has been to assess separately the effects of the operation on five different facets of the personality, determinants of five different parts of everyday behaviour. Such an analysis reveals the pattern of the adaptation of the leucotomised patient in his total environment, and the ways in which he fails to achieve the normal. The patients who form the material for this study were all operated on at Runwell Hospital by Mr. G. C. Knight, mostly between 7 and 3 years ago. Every patient has been watched personally by one or other of us over the whole period, and those outside hospital have been seen sometimes in their own homes. In addition, relatives have been seen by one of us or our psychiatric social worker. The report is not a cross-section of the results of follow-up on one occasion but a summary of our findings and records over a long period. We have assessed the psychiatric clinical picture, the civil and social status, the ability to work, the capacity for pleasure, and the loading of the patient with socially objectionable personality deficiencies.

For the purposes of this study the patients have been divided into two broad groups, C and A, on the basis of their preoperative condition. Group C contains the chronic severely disordered psychotics in the mental hospital, about half of them having schizophrenia, and the other half paraphrenia, epilepsy, chronic mania, or depression. All of them had the very worst psychiatric prognosis. Group A contains the patients admitted to hospital specifically for the operation—e.g., patients with severe neurotic depression, obsessive-compulsive neuroses, and chronic tense hypochondria—all with severe symptoms accepted as an indication for operation. In other words this group consists of patients whose contact with reality, either in duration or in mental state, was not remote. However, the difference between the groups relevant to this study is essentially this: group C corresponds to those patients whom nowadays we operate on primarily to ameliorate severe behaviour disorder, for "nursing improvement," whereas group A corresponds to those operated on primarily to secure complete social rehabilitation.

We tabulate below the results of our analysis with 100 cases of group C. For clarity we have given to each grading a short title. These are merely labels for the standards which we have adopted and which it is necessary to define at some length. We regard this as very important. Halstead (1946) has thrown down the challenge that no attempt has been made to standardise the criteria for the preoperative and postoperative status of leucotomised patients. Ours is far from an attempt to standardise criteria, but we hope to leave no ambiguity in the meanings we convey.

Group C (100 cases)

Illness:		*Work:*	
Cured	9	Full	3
Much improved	24	Partial	8
Improved	25	Self-occupied	37
No better	36	None	52
Worse	6	*Pleasure:*	
Status:		Full	4
Social recovery	13	Partial	29
Discharged home	17	None	67
Social upgrading	27	*Bad Features:*	
No better	73	Dominant	20
Dependent	43	Present	36
		None	44

Illness.—Under the term "illness" we have assessed the patient clinically on his psychiatric symptoms. This grading shows the effect of leucotomy on the mental illness for which the patient was operated. Starting with the clinical features which constituted the preoperative psychosis, we have considered what has happened to these features without reference to the general social adaptability. However, this must not be interpreted too narrowly. For example, if a chronic schizophrenic who made frequent violent attacks on other patients and nurses shows very little change in the psychosis except that he now no longer makes violent attacks he will be graded "improved," though the change is observed in his behaviour as it affects others. The gradings correspond qualitatively to those in common usage; this was our intention.

In the "cured" category the illness has cleared completely; all the major symptoms and signs have disappeared, and it is impossible to make out even the skeleton of the original psychosis. All these patients were discharged.

Under "much improved" are included some severely disordered patients who have lost most of the overt signs of their psychosis and have regained contact with reality to a considerable extent. Their residual symptoms are inconspicuous. This category also includes those cases in which there has been complete removal of all dominant symptoms and signs, and of the accompanying distress and suffering—a change like that which takes place after operation in cases of unbearable physical pain. The persisting symptoms seem inert and lack forcefulness or tension.

Under "improved" we have placed the remaining patients in whom there is some obvious change for the better. It may be a slight over-all improvement in the intensity of their illness; the disappearance of some features without the appearance of others; or a lessening in intensity of any of the dominant preoperative features.

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Similarly, if these phenomena occurred in reverse we graded the patient "worse."

Status.—Under "status" it is the social level and adaptation which are graded. "Social recovery" implies that the patient is living in his own home, at ease with his family; that he takes part in everyday activities outside his home, in harmony with his fellow citizens; and that he is a satisfactory social fit. Secondly we have recorded that 17 patients were discharged, for this fact alone is not a sufficient indication that the patient is a social recovery. What we have assessed here is the status the patient has actually achieved, rather than his acceptability. Some of those who achieve a smooth uneventful existence outside hospital may have some very undesirable character traits. Altogether there are 27 who have achieved some higher level of social existence. If an impulsive hallucinated schizophrenic, previously in a refractory ward, is now living continuously in a better or open ward, his status is improved. The total clinical picture may, however, be equally psychotic. On the other hand, the patient may be psychiatrically much improved and yet, because of a single behaviour trait, unfit for a better ward, convalescence, or complete discharge. In leucotomised patients the two aspects do not necessarily go hand in hand. There is no improvement in 73 patients, of whom 43 are completely dependent on others for their daily existence. All patients in chronic mental-hospital wards are, by some definitions, dependent; but these patients need constant supervision and have to be restrained, fed, dressed, or washed, and cannot, or will not, look after themselves.

Work.—"Full" stands for ordinary full employment of the sort the patient was accustomed to. If he does the job up to normal accepted standards, with a fairly liberal interpretation, he is graded "full." He is not so graded, however, merely because he attends regularly at some place of work, since this would only confuse his work status with his ability to do the job. If there is such a discrepancy, it is reflected in his category under "status." "Partial" stands for partial employment, the performance of obviously substandard work, even though this may take place over a full working week, or any occupation other than fully paid work. "Self-occupied" perhaps might better be called "self-amused," since it is a category of patients who occupy their time by trifling and ineffective activities, not useful for others and never worthy of the title "work." "None" stands for those who do nothing.

Pleasure.—Under "pleasure" we have assessed the patient's capacity for enjoyment, his general happiness and ability to make himself happy from what life offers, and the extent of his desire for play or pleasurable activity. We have been concerned with the active enjoyment of entertainment and social intercourse, of reading and music, and all the pleasurable activities of the daily and weekly round. What is lost after full leucotomy is the appreciation of the pleasure previously derived from these things; the higher happiness and joy which complete the full life of a human being are absent. We are not concerned with the more elementary psychological concept of pleasure at the instinctive and vegetative level. This is impossible to assess properly. In some cases it appears to be enhanced by leucotomy. Our grading refers to the real capacity for pleasure and joy. "Full" signifies its normal presence; "none," its absence; "partial" the broad range between. Those in this category were evenly distributed between the two extremes.

Bad Features.—Under "bad features" we refer to unpleasant objectionable behaviour traits. In the first category we have placed those which were so pronounced as to dominate one's whole impression of the patient. In C cases such features may be residual psychotic symptoms, but in the 20 cases graded "dominant" there were 9 in whom pressing signs, such as extreme gluttony and volubility, were definitely post-leucotomy features. In a further 36 cases there were some antisocial behaviour characteristics which were so noticeable or so severe as to constitute a permanent nuisance or objectionable feature. We are aware that the presence of these features cannot bear much weight in patients who were originally so psychotic. The striking fact, however, about these figures is the discrepancy between the distributions in the five main divisions.

SIGNIFICANCE OF EARLY RESULTS

The number of purely psychiatric improvements, over 50%, is very encouraging and agrees with those reported by other workers and with our own early results. At this point it is pertinent to make it quite clear that we do not suggest that the time has arrived to question the value of prefrontal leucotomy in severe chronic psychotics. The time has come to realise precisely how much the operation achieves; or how little, in the way of ultimate social advantage; and to hope that this limited and unilateral recovery may be achieved by a less gross surgical procedure than that now commonly used. Even if the present confusion in the clinical field is only one of a differing terminology among many workers, we should try to clear it by recording a greater number of objective facts, rather than to add to it by increasing the number of psychopathological theories. When the terms "cured" or "improved" are employed in medical and psychiatric practice, it is usually implied that the illness of the patient is relieved so that he can resume normal citizenship in work, play, and social activities; or at least that he has recovered these natural attributes to a degree in keeping with the relief from his illness. This is the common usage, and the fact that divergence from this gives wrong impressions is recognised, for example, by the cliché "the operation was a great success, but the patient died." In surgery one is neither entitled nor expected to talk of cure merely because the tumour has been removed.

Group A (25 cases)

Illness:		*Work:*	
Cured	10	Full	2
Much improved	9	Partial	4
Improved	4	Self-occupied	12
No better	2	None	7
Worse	0	*Pleasure:*	
Status:		Full	3
Social recovery	11	Partial	11
No better	14	None	11

Bad Features:	
Dominant	3
Present	15
None	7

We now turn to the A cases. In grading them we have adopted the same standards as for the C cases, but there are one or two points worth mentioning. The nature and quality of the patient's work, and his reactions to opportunities for pleasure, have been examined with some care. If a skilled electrical engineer is now employed full-time in his old factory, but as a cleaner, and if he is sometimes absent and only holding on to his job through the kindness of his old employers, he will properly be graded "partial." In such a case superficial inquiry might show him to be in fully paid employment. All cases graded "partial" have had a similar gross falling off of ability. It is not that they have merely lost some of the finer skills and judgment required for their original job. If this were the only type of loss, and they were employed at their original work, even with some loss of efficiency, they would be graded "full."

The other point arises under "bad features." Here again the standard compared with the C cases has not been altered. With A cases, however, all these features are the result of leucotomy. They are severe

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and unpleasant antisocial traits; and by definition none of the A cases had them before operation. It was, in fact, for group A that we introduced a grading of bad features. They include gross tactlessness, apathy and inertia, excessive volubility, greediness, deceit, rudeness, egocentricity, marked coldness of emotional response, spitefulness, and absence of sympathy, tolerance, and kindness. After leucotomy all patients suffer some personality defect. They are graded present only if they are so prominent as to be objectionable to all ordinary lay people, and to make the psychiatrist wonder if the operation was worth while.

The results are now summarised and expressed as percentages. The term "relieved" is used for "cured" and "much improved," and we think it describes fairly the effect on the illness. "Little change" includes the remaining three categories:

	C	A
Illness:		
Relieved	33	76
Little change	67	24
Status:		
Recovered	13	44
No change	73	56
Work:		
Full or partial	11	24
None	89	76
Pleasure:		
Full or partial	33	56
None	67	44
Bad features:		
Present	56	72
None	44	28

Looking at these figures we see that, while 33% of the C cases have been relieved of their illness, 89% are still not employable. Two-thirds are unable to enjoy their ordinary pleasures, and over half of them harbour severe antisocial features. One wonders whether a similar social result, though with a different qualitative pattern, could not be obtained with intensive application of other treatments, such as electric convulsions or insulin shock.

With the A cases the comparison is more pronounced: 76% are relieved of their illness (again agreeing with the results of other workers) but only 44% recover a full social status; 76% cannot work; 44% do not enjoy their original pleasures; and 72% are handicapped by objectionable antisocial personality deficiencies. Only 8% are in full remunerative employment, and 12% getting their full share of pleasure. These are people whose potentiality before their illness was normal in all these respects and who had no personality defects of the kind we refer to. These figures may be given a little colour by three illustrative case-records.

THREE CASES

Case 1.—A married woman of 49, a melancholic with severe obsessional features. It began with classical symptoms of never being sure whether she had locked the door or turned off the tap. Six weeks before admission symptoms became acute, for the second time. If anyone became ill or died, she was sure it was her fault. She was convinced that she had given the family venereal disease, and that the police were about to arrest her for a murder. She would send her husband down in the middle of the night to make sure the windows were shut, though he had to put on his wooden leg. She told her husband that her youngest son was by another man, and that she had hit her grandchild on the head. She wept, became extremely agitated, and threatened suicide. She said the food and the bed-clothes were full of germs, and her last instruction before leaving for hospital was that her husband should burn the pillow-slip.

She has been freed from all these symptoms. She is cured of all compulsive acts. She lives at home, and rises early in the morning without fear of infection, without worrying over marks in the teacup, and without compulsive repetition of every act. She has been cured of her obsessional illness.

She is, however, no better off. She is completely ineffective for a different variety of reasons, and she is distressed by her inadequacy and failure. She finds herself quite unable to plan or to think out how to do the simplest of jobs. She is extremely voluble, and sometimes talks in a torrent of words, with complete inability to express what is in her mind. She feels flurried and rushed, and realises she must get such and such a thing done quickly; but she never does anything. She simply cannot manage her affairs. She is restless and expends colossal energy on tiny tasks, but never finishes. Consequently she is too tired to go out for pleasure. She intends to, but when the time comes is too apathetic. She never feels able to enjoy anything. Previously a regular picture-goer, she has never been since operation. In any case she is over-talkative, gluttonous, and muddled, and jars on everyone. In brief, she is not acceptable in company. She has been reduced to a restricted and ineffective existence, pleasureless for herself, objectionable to others.

Case 2.—A woman of 66, with a severe agitated melancholia of 4 years' duration. She was extremely depressed, restless, and confused. She showed no interest in anything and would occasionally strike out at other patients. She rarely said anything, and then only in a whisper.

The operation cured her illness. There have been no signs of agitation or depression, and her energy seems inexhaustible. If she undertakes a job in the house she carries it through, no matter how inconvenient the time, or how much nuisance she is to the others. She is always laughing, often inappropriately, showing no consideration for sorrow or ill health, unmoved by any catastrophe. Her activities are never a help but always a hindrance. In Freeman's terminology; she is not conscious of the relationship of herself to her own environment. She is coy with men, and giggles like a little girl, peeping round doors at them. She harbours severe antisocial features, making her quite unacceptable. She is excessively voluble, overbearing, selfish, conceited, irritatingly argumentative, and excessively obstinate—all traits never seen in her before leucotomy, when she was a gentle and generous character. Now she is entirely egocentric, bluntly tactless, and inclined to lie and deny having done her foolish acts. Furthermore she wets the bed and has been incontinent in the living-room. Her appetite is tremendous; she literally gorges, often spilling food on the floor. If people will not listen to her or let her have her way, she becomes noisy, rude, and aggressive. She completely denies her faulty habits. Her relatives have been worn out by her hard and unbearable attitude. They say that for her the operation may have been miraculous, but they wish they had not got to live with her. This patient has become a grossly unpleasant personality incapable of any useful activity, and a severe misfit from a multitude of antisocial features.

Case 3.—A married man of 52, with an obsessive-ruminative neurosis of some years' duration. He became much worse in the last year, with anxiety, depression, and agitation. His mind was full of pseudophilosophical, sexual, religious, and blasphemous thoughts. When he attended a religious service he could not get sexual ideas out of his mind. He was afraid of travelling. The word suicide kept coming into his mind. He became very self-critical and self-depreciatory, tense, agitated, and restless.

Since operation all phobias and morbid ruminations have disappeared. He says that an occasional thought may float into his consciousness, but he is not troubled by it. Objectively it is obvious that the agitation, pathological preoccupation, and emotional tension have been eradicated.

However, he feels no better though he no longer has his ruminative neurosis. His face is expressionless. He is apathetic, lazy, and sometimes depressed. He cannot concentrate or plan, and his memory has failed. He has lost all initiative, and he cannot manage his business affairs, or even make the effort to get out to the theatre. He does go out for walks, and he goes along to his old club, both activities being long-established habits. He says he gets on well with the others, but this opinion conflicts with that of his colleagues. He was once a vital personality, holding the floor and standing up to anyone. Now he takes a back seat, never cracks a joke, cannot take leg-pulling, and has lost all joie-de-vivre. He has little judgment or discrimination, and behaves in a detached and solitary fashion. His manners and personal habits have deteriorated. He is irritating, rude, and tactless, all without insight. He occupies himself with a little gardening, but even this seems too much effort. He has been relieved of his original illness, but is now reduced to a very restricted existence, with a profound reduction of capacity for work and pleasure and impairment of all those finer qualities which go to make a successful social fit.

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WEIGHING UP THE RESULTS

The doubts reflected by our figures have been echoed at the Scandinavian Congress at Copenhagen in 1946. Rylander, talking of cases of a well-preserved type, remarked:

> "The extremely troublesome symptoms for which the operation was performed, disappeared. One is tempted to regard the operation with unrestricted enthusiasm. Unfortunately, closer examination of the patients reveals that the operation was followed by undesirable changes."

Wohlfahrt (1946), referring to psychotics, says:

> "It is distinctly hazardous to leucotomise schizophrenics. Difficult as it is, clinically speaking, to judge the complex and conflicting factors of mental disease and character which combine to produce the existing schizophrenic picture, where deep-seated symptoms may be covered by autistic thinking, it is still more difficult to foresee what is going to happen when we proceed to eliminate one of the components in this labile equilibrium, notably the emotional tension. . . . The risk of operation seems relatively small. A greater danger is the possibility of producing mental invalids. It is scarcely conceivable that leucotomy can be adopted for many years to come as a routine method of hospital work."

We believe, however, that for some schizophrenics, provided they have not responded to other treatments and have the worst prognosis, leucotomy is at present justified for the results obtained.

It is therefore in the A cases that Wohlfahrt's possibility of mental invalids becomes a serious and halting consideration. It is in these cases that good must be weighed against bad with great care. Certainly there are some in whom the advantages of operation are outweighed by damage to the personality.

In the A cases the percentages of 76, 44, and 72, against work, pleasure, and bad features, must be regarded as a net loss due to the operation. It has been said that the better the personality the better is the operative result. Certainly, if we leucotomise a patient with a stable and highly integrated personality, we may end up with a better person than if we start with a previously poor personality with the same illness. This does not mean that a good personality is an indication for operation. We believe that the patient with a good prepsychotic personality will suffer much more loss than will a patient with a simple and shallow personality in one of the more lowly occupations. In medicine it is our duty to consider the benefit to the individual patient. If a good personality has relatively more to lose, we should be less ready to recommend the operation for him. We do not deny that after operation he may still have a better personality than the patient with a poor prepsychotic personality; but this will be of no comfort to *him*.

CONCLUSION

There is a tendency to move away from indiscriminate attack on all severe psychotics of hopeless prognosis. There is increasing use of leucotomy on sane and well-preserved patients, with "specific" indications, in the belief that this is a more scientific and less empirical procedure. We suggest that this tendency is wrong, and that the only unequivocal indications seem to be in chronic psychosis with severe disorder of behaviour, and in chronic intractable obsessional and depressive states with prolonged and total incapacity. While the technique is so relatively crude, it is not certain that in other cases there is a net gain. Great caution combined with careful judgment must be used in selecting cases from the better type of patient.

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MACROCYTIC ANÆMIA IN CENTRAL AFRICANS

IN RELATION TO ANCYLOSTOMIASIS AND OTHER DISEASES

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Trowell's pioneer work has clearly shown iron-deficiency anæmia in Uganda; he also found a macrocytic anæmia, the nature of which is less understood (Trowell 1942, 1943, 1947).

In the present inquiry 44 cases of severe anæmia were investigated.

There was no special selection, except that the age of the patients was above 12 years and the hæmoglobin level below 7 g. per 100 ml. In 32 cases there was an iron deficiency, the nature of which is discussed below. In 12 cases no iron-deficiency anæmia was seen on admission; these patients had malaria or bacterial infection either alone or complicating ancylostomiasis. Of the women 5 were pregnant, but there was no difference in the pattern of their disease from that of other patients in this series. The average stay in hospital was $2^1/_2$ months, and no patients were discharged unless they had reached normal hæmatological values. There were 4 deaths, and 4 patients absconded from hospital before they were fully cured.

In 22 well-nourished Central African men the hæmoglobin level was 13·9–18·35 g. per 100 ml., and in 5 well-nourished Central African women 14·0–15·7 g. The red cells of the men numbered 4,900,000–6,100,000 per c.mm., and those of the women 4,900,000–5,100,000. The mean corpuscular volume (M.C.V.) in all 27 cases was 82–92 c.μ, and the mean corpuscular hæmoglobin concentration (M.C.H.C.) 31·9–36·8%. In 14 of the 27 patients the plasma volume was determined; the plasma volume, blood volume, total circulating hæmoglobin, serum-protein, serum-albumin, and serum-calcium all fell within the limits considered as normal in Europe and in India. Of the 27 well-nourished Africans 6 had sickle cells; and so had 7 of 44 anæmic Africans with a hæmoglobin level below 5 g. per 100 ml. Hence there seems to be no significant difference between the incidence of sickle cells in well-nourished and that in severely anæmic Africans. I hope to publish jointly with A. Milne evidence obtained in a mass investigation that the sickel-cell trait is equally distributed in anæmic and in non-anæmic Africans.

METHODS

This paper is a summary of work on anæmia rather than a full report. It does not contain full details of hæmatological technique or of therapeutic measures.

Hæmoglobin.—The hæmoglobin was measured in three different ways: alkaline hæmatin, acid hæmatin, and cyan-hæmatin. Cell-counts were done in quadruplicate with mercury-calibrated pipettes. Cell volumes were determined by centrifuging heparinised blood for 30 min. at 3000 r.p.m. Reticulocytes were stained with azur II. Plasma volume was determined with Evans blue.

Diet.—All patients received the Mulago stock diet, which contains as staple carbohydrate either cooked bananas (matoke), sweet potatoes (lomonde), or rice. Main sources of protein are beans and groundnuts and 4 oz. of meat thrice weekly. My patients received in addition 8 oz. of meat, 12 oz. of milk, and 8 oz. of bread daily. Thus any failure in improvement of an anæmia could not be ascribed to too low an intake of calories or of animal protein. It was necessary to give to all patients twice daily 200 mg. of ascorbic acid; the iron therapy included this amount of vitamin C; and, since results had to be clearly due to iron, ascorbic acid had to be given as a control in all cases.

Iron Medication.—This was as follows:

Twice daily 4 tablets (50 mg. each) of ascorbic acid.
Twice daily in orange water: Ferri sulph gr. 20.
Glucose gr. 48.
Acid. hydrochlorici dil. *B.P.* min. 5.
Aquæ chloroformæ ad fl. oz. 1.

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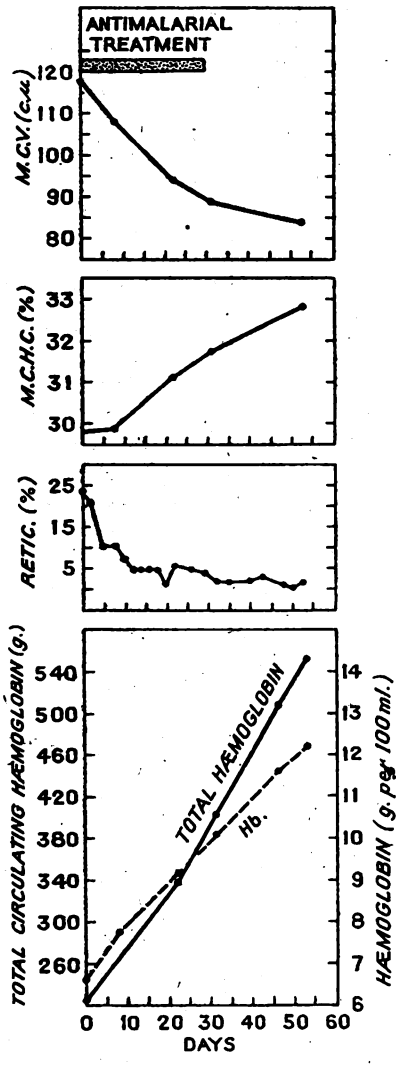

Fig. 1—Correlation between macrocytosis and reticulocyte percentage in malarial anæmia in an African woman aged 35.

Hookworm Purge.—This was carried out as follows: at 8 A.M., fasting, carbon-tetrachlorethylene 4 ml. and oil of chenopodium 2 ml. were given on solid sugar. After 2 hours magnesium sulphate 8–12 g. was given in a copious warm draught. Magnesium sulphate was repeated at 12 noon. No food was allowed until two stools had been passed. At 7 P.M. 7 oz. of sugar dissolved in water and 8 units of soluble insulin were administered to forestall any possible liver damage. Even in very weak patients no ill effects were seen after this treatment.

RETICULOCYTOSIS AND MACROCYTOSIS

Fairley et al. (1938) pointed out that malaria accompanied by hæmolysis and reticulocytosis might be involved in the production of nutritional macrocytic anæmia, and Wintrobe (1934) showed an increase in M.C.V. in pernicious anæmia, coinciding with the increase of reticulocytes, when treatment was instituted. He later showed that the increase of M.C.V. on iron treatment in chronic hypochromic anæmia also coincided with the reticulocyte response, but the cells did not then become macrocytic (Wintrobe 1946).

Not much attention has been given hitherto to reticulocytes as a possible cause of macrocytosis in Central Africa; yet the outpouring of reticulocytes from the bone-marrow seems to be the usual cause of macrocytosis in this part of the world.

Reticulocytes are larger than the normal circulating cells; but, in contrast to the megalocytes of pernicious anæmia and of the nutritional macrocytic anæmia of Wills, reticulocytes have a normal mean corpuscular hæmoglobin (M.C.H.), and their M.C.H.C. is consequently low. Thus the presence of many reticulocytes and of cells in an early postreticulocytic stage will produce a picture of macrocytosis with hypochromia.

In Malaria.—Fig. 1 shows recovery from macrocytic anæmia in malignant tertian malaria. The reticulocyte percentage, which was high on admission, fell on mepacrine treatment, the M.C.V. returned to normal, and the M.C.H.C. rose. No treatment with hæmatinics was given throughout the period shown in fig. 1. After 60 days the hæmoglobin level remained stationary at 12 g. per 100 ml. for 12 days, and after the removal of 328 hookworms, followed by iron treatment, it started to rise again. After a further 14 days the patient was discharged with a hæmoglobin level of 13·9 g. per 100 ml. and red cells 4,787,500 per c.mm. Within 86 days in hospital the total amount of circulating hæmoglobin had risen from 256 to 629 g.

In Other Infections.—Similar macrocytic anæmias with a high reticulocyte-count, a normal M.C.H., and a low M.C.H.C. can be seen in other infections in Africans, particularly in pneumonia. As in malaria, so in these infections on specific therapy without hæmatinic medication the reticulocyte-count falls, the anæmia improves, and the M.C.V. returns to normal, with a corresponding rise in M.C.H.C.

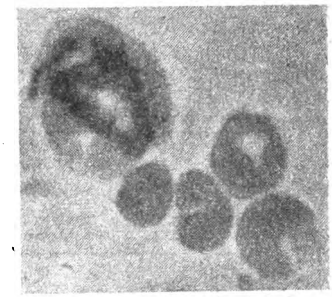

Fig. 2—Dual cell population in blood 3 days after start of iron therapy. Large cell is a reticulocyte.

IRON-DEFICIENCY ANÆMIA

The great majority of untreated cases of iron-deficiency anæmia show no macrocytosis. The M.C.V. is either normal or (in about a third of the cases) less than 75 c.μ. The M.C.H. and M.C.H.C. are usually low. These cases of hypochromic anæmia differ from those seen in Europe inasmuch as the red cells usually number less than 2,000,000 per c.mm. and not uncommonly less than 1,000,000 per c.mm. Further, the percentage of reticulocytes is raised (about 5%), though the absolute reticulocyte-count may be less markedly increased (60,000–120,000 per c.mm.).

Pattern of Recovery

On treatment with ferrous sulphate gr. 40 daily a pattern of recovery results which again differs from that seen when hypochromic anæmia is similarly treated in Europe (table I).

Within a week a high reticulocyte-count of 25–45% can be observed and the blood smear shows a dual cell population of old cells and new macrocytes (fig. 2). At the same time there is a considerable increase in the M.C.V. and M.C.H., but the M.C.H.C. remains at first stationary, or may even fall. In some cases at an early stage it is possible to show on vital staining that all the

TABLE I—PATTERN OF RECOVERY FROM IRON-DEFICIENCY ANÆMIA IN CENTRAL AFRICA

Stage	Hæmoglobin percentage	Red-cell count	Reticulocytes (%)	M.C.V.	M.C.H.	M.C.H.C.
Admission; starting on Fe therapy	Low	Low	2–10	Usually normal	Low	Low
1st week ..	Rapid rise	Almost stationary	12–40	Rapid increase	Increase to almost normal	Stationary
4th week ..	Continued rise	Rising	12–18	Decrease	Normal	Slowly rising
4th–8th week	Gradually becoming stationary	Gradually becoming stationary	4–10	Slightly above normal	Normal	Slightly below normal
			Anthelmintic treatment			
8th–12th week	Rising to normal	Rising to normal	0·5–2	Return to normal	Normal	Rising to normal

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new cells are reticulocytes, but, as time goes on, the proportion of reticulocytes among the large cells declines. These new cells were first observed by Trowell (1942), and it has been suggested that they were the megalocytes of nutritional macrocytic anæmia. If this was so, they should be very well, or even maximally, hæmoglobinised, and there is no doubt that in blood smears stained with Leishman the macrocytes take on a darker colour than do the old cells. This, however, is due to a blue hue produced by the basophilic substances present in young cells. In blood smears stained with eosin alone no difference in depth of colour can be seen in the two cell populations. Another reason for considering these large bluish cells as megalocytes has been the finding of megaloblasts in the bone-marrow at this stage. These were not seen in the present investigation, and Trowell (1947) has clearly stated that the presence of a megaloblastic bone-marrow can no longer be assumed. Nevertheless, megaloblasts in the bone-marrow are the sine qua non for megalocytes in the peripheral blood. The differences between the megalocytes of nutritional macrocytic anæmia and coctic cells are given in table II.

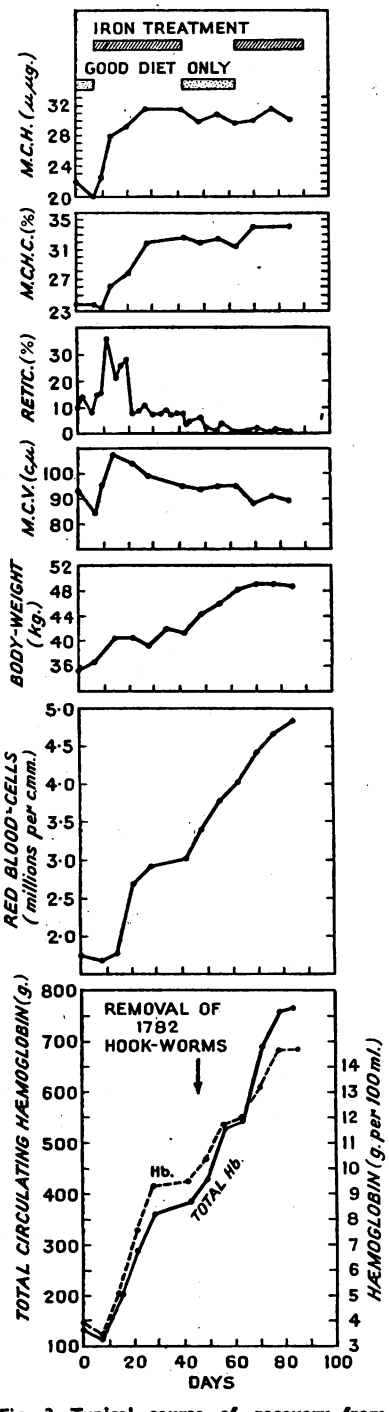

Fig. 3—Typical course of recovery from hypochromic anæmia in an African man aged 22. Rise in M.C.V. is definite but not spectacular. Number of hookworms removed probably represented entire load carried. No ancylostoma ova were found in stools tested weekly after purge, either in direct preparations or by flotation method.

The reticulocytes and cells in the early postreticulocytic stage are here called coctic cells. By coctic blood picture is meant one due to a condition where large cells are produced in regeneration, the macrocytosis not being due to a disturbance of bone-marrow function by the absence of essential nutrients but being, on the contrary, caused by a hyperactivity of the marrow which leads to an emission of slightly "unfinished" cells (*coctus* = fully mellowed). To call these cells immature might suggest an inhibition of cell production at the nucleated stage, and the term "regenerative" would not differentiate from a state where regeneration proceeds without macrocytosis.

The profound and rapid effect of iron treatment on the M.C.V. may explain why microcytic hypochromic anæmia is less common than in Europe. Complications by infections and malaria are the rule, and the iron released from destroyed cells should be available for the production of larger coctic cells. On the other hand, the incidence of macrocytosis in newly admitted patients will be greatly overrated if those who have previously received iron treatment as outpatients are not excluded.

While the change from normocytosis to macrocytosis takes place there is a discrepancy between the rates at which the amounts of hæmoglobin and of red cells increase. It will be seen in fig. 3 that a week after iron treatment was begun the hæmoglobin level had risen by 50%, whereas the number of red cells had increased by only 6%. This phenomenon is reflected in the blood films. The old cells with a low M.C.H. rapidly disappear,

TABLE II—DIFFERENCES BETWEEN MEGALOCYTES OF NUTRITIONAL MACROCYTIC ANÆMIA AND COCTIC CELLS

Findings, &c.	Megalocytes	Coctic cells
Percentage of reticulocytes	Low	Raised
M.C.V.	From little above normal to very high (>140 c.μ.)	From normal to fairly high (rarely >130 c.μ.)
M.C.H.	High	Usually normal, but can be raised above normal
M.C.H.C.	Within the higher levels of normal	Below normal, rarely reaching lower limits of normal
Bone-marrow	Megaloblasts; perverted development	No megaloblasts; normoblastic marrow
Cause of cell enlargement	Disturbance in bone-marrow of blood production at nucleated stage	Rapid outpouring from bone-marrow of not fully mellowed cells, possibly also a direct effect of parasites on reticulocyte ripening
Recovery on	"Wills' factor," liver extracts, yeast preparations, folic acid, thymine, vitamin B_{12}	Removal of factor causing peripheral blood-loss which is responsible for hyperactivity of bone-marrow

which suggests a fast turnover of the cell population. The new coctic cells gradually take the place of the old cells entirely, and this fact explains why their appearance should have such an exaggerated effect on the mean absolute values, and why the rise in M.C.H. and M.C.V. should be pronounced while the red-cell count may remain stationary.

As time goes on, the blood picture becomes less macrocytic. This might be explained by shrinking of the circulating coctic cells (E. Jacobsen, personal communication). Within 4–6 weeks a stationary phase is reached. Further iron treatment will not improve the anæmia. This later resistance of an iron-deficiency anæmia to iron therapy has been clearly reported by Trowell (1943). At this stage the amounts of hæmoglobin concentration and of red cells remain more or less stationary, the M.C.V. remains near the upper limit of normality, the M.C.H.C. continues to rise slightly though it rarely reaches normal, and the M.C.H. continues to improve within normal limits. The percentage of reticulocytes at this stage is lower than it was at the beginning of the coctic phase; however, if the increased number of red cells is taken into account, it will be seen that the absolute reticulocyte-count has not greatly fallen. This implies that there is no lessening of bone-marrow activity

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TABLE III—DEVELOPMENT OF A MACROCYTIC NORMOCHROMIC ANÆMIA IN A CENTRAL AFRICAN, AGED 40, ON FERROUS SULPHATE GR. 20 B.D.

Blood-findings	Admission	4th day	7th day	11th day	18th day	32nd day	39th day	46th day	51st day	58th day	65th day
Hb (g. per 100 ml.) ..	2·02	2·39	4·06	4·93	6·24	8·42	8·90	9·30	9·50	9·10	9·43
M.C.V. (c.μ)	88·7	100·0	124·0	132·0	123·5	107·0	110·0	104·5	110·0	114·0	122·0
M.C.H. (μμg.).. ..	18·1	21·7	29·4	33·1	33·6	30·9	31·6	30·4	31·6	32·9	35·3
M.C.H.C. (%) ..	20·4	21·7	23·7	25·1	27·1	28·7	28·7	29·1	28·8	28·8	29·0
Reticulocytes (%) ..	7·06	9·8	18·6	25·7	17·5	2·8	3·0	3·9	4·7	3·5	4·0

at this stage, and that some destructive process must be keeping pace with the outpouring of new cells.

Some patients left for longer than a month in this condition, and liberally supplied with iron all the time, may show once again a gradual increase in M.C.V. Presumably the new coctic cells become larger, according to the regulating mechanism which determines that reticulocytes are always larger than the circulating cells. There is thus a gearing up into macrocytosis with high M.C.H. values, but the fact that the M.C.H.C. remains always at the lower level of normality easily separates this picture from that seen in nutritional macrocytic anæmia. Additional differences are that megaloblasts are absent from the bone-marrow, and that the relative reticulocyte-count is raised. In table III details are given of a case developing into an almost normochromic macrocytic anæmia, and it will be seen that the M.C.H.C. of 29% and the raised relative reticulocyte-count differentiate the coctic picture from that of nutritional macrocytic anæmia.

Full Recovery on Removal of Hookworms

The stoppage of recovery on iron treatment usually takes place when the hæmoglobin is 9–12 g. per 100 ml. Further progress takes place on anthelmintic treatment (fig. 4), and it is astonishing to see patients increase their circulating hæmoglobin by as much as 500 g. in 4 weeks while carrying 300–4000 hookworms in their intestines. There is no correlation between the hookworm load and the level of hæmoglobin at which the anæmia ceases to respond to continued iron treatment—i.e., the degree of anæmia at which the hookworm anæmia has been divorced from its iron-deficiency factor.

On worming, the hæmoglobin level will rise even if iron treatment is discontinued (fig. 3), but at this stage the body seems to contain only about 300 mg. of iron as a reserve for the formation of additional hæmoglobin. After an increase by about 2 g. of hæmoglobin per 100 ml., or 100 g. of circulating hæmoglobin, iron treatment has to be reintroduced to enable the patients to produce a fully normal amount of hæmoglobin.

HOOKWORM ANÆMIA WITHOUT IRON DEFICIENCY

The facts that during the "stoppage" stage a hookworm anæmia exists without signs of iron deficiency, and that with a liberal supply of iron the macrocytosis may become more and more pronounced (table IV), lead to an understanding of cases of anæmia which come into hospital, some with a considerable macrocytosis, and all with a raised percentage of reticulocytes, normal or increased M.C.H. and M.C.H.C. at the lower level of normality (table V). These patients invariably have or recently have had, malaria or bacterial infection, and it must be assumed that they have reached a stage where more blood-cells are destroyed by these superadded diseases than are produced by the bone-marrow. Thus more iron becomes available for the new cells, and what had been an iron-deficiency anæmia at a higher red-cell concentration has been converted into an anæmia with normal M.C.H. The hookworm anæmia presents then a picture seen during the first stage of iron treatment, but in these cases the iron is derived from a surplus of intravascularly destroyed cells. The increased M.C.H. excludes iron deficiency as the cause of the anæmia, and the relatively low M.C.H.C. and the raised reticulocyte-count distinguish the picture from that of nutritional macrocytic anæmia. On treatment of the malaria or bacterial infection, little or no progress will be achieved unless anthelmintic treatment is instituted as well. As during the treatment of some cases of pernicious anæmia, so in these cases iron treatment will have to be introduced at a later stage, since the body does not carry sufficient iron for full recovery. In one case no need for iron therapy arose until the circulating hæmoglobin had increased from 176 to 592 g.

ALTERATION OF RECOVERY PATTERN BY ANTHELMINTIC TREATMENT

Table VI shows that the recovery from iron-deficiency anæmia followed more closely that seen in Europe when anthelmintic treatment had been carried out before the iron treatment was begun. As shown by Wintrobe (1946), even in uncomplicated hypochromic anæmia a moderate increase in M.C.V. coinciding with a rise in reticulocyte percentage will then take place.

EFFECT OF WORMING ALONE ON HYPOCHROMIC ANÆMIA

On treatment of hookworm infestation alone without any iron medication the hæmoglobin level in iron-deficiency anæmia will rise by 1–2 g. per 100 ml. This is not due to a change in plasma volume, which is supposed

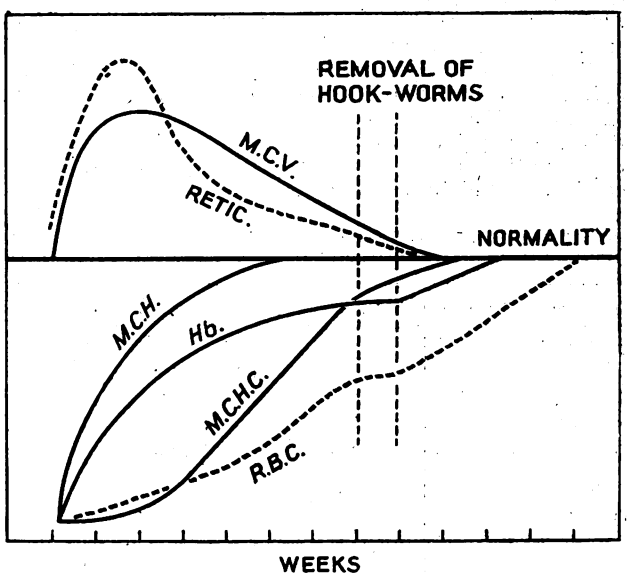

Fig. 4—Pattern of response of hypochromic anæmia at first to iron and later to worming. The various absolute values rise and fall differently with the result that a normocytic or microcytic hypochromic anæmia changes on iron therapy to a macrocytic anæmia, which can be cured only by removal of hookworms.

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to be particularly high in ancylostomiasis, and the increase of hæmoglobin is paralleled by an increase in total circulating hæmoglobin by 50–100 g. However, the M.C.H.C. and M.C.H. will remain low, whatever diet is supplied. Table VI shows the progress of a patient who was wormed before he was treated with iron. The amount of circulating hæmoglobin fell by 36 g. in a week before the removal of 824 hookworms. It rose subsequently, while iron therapy was withheld, by 44 g. in a week. It may therefore be assumed that the real loss before worming was 80 g. of circulating hæmoglobin a week. The hæmoglobin level being 4·2 g. per 100 ml., it can be calculated that one hookworm removed 0·33 ml. of blood a day, and in other cases very much higher values were obtained.

IRON-DEFICIENCY ANÆMIA A SEQUEL OF ANCYLOSTOMIASIS

Three findings seem to indicate that the iron-deficiency anæmias at Mulago hospital—and they are the great majority of anæmias amongst the adults—are due to hookworm infestation: (1) iron cannot fully cure an iron-deficiency anæmia, though it may produce a normochromic blood picture; (2) hookworm anæmia can exist without iron deficiency; and (3) iron-deficiency anæmia will for a time respond favourably to the removal of hookworms alone. No nutritional macrocytic anæmia was found among the 44 cases of severe anæmia studied; and, since the iron-deficiency anæmia was due to parasites, the final cure of these anæmias depended on the removal of causes of peripheral blood-loss rather than on medicines supplying essential nutrients to the bone-marrow.

ANCYLOSTOMIASIS AND SKIN COLOUR

A striking observation is that the removal of hookworms not only restores the arrested recovery from anæmia but also abolishes symptoms usually associated with kwashiorkor, such as pale skin, straight hair, and swollen parotid glands. The skin usually darkens by anything from 3 to 12 von Luschan skin-colour units within a few days, and the hair curls within two or three weeks. The effect of worming on skin colour can only be seen in patients whose iron-deficiency anæmia has been previously corrected. If a patient with iron-deficiency anæmia receives anthelmintic treatment, the rapid darkening of the skin will not be seen; but it will set in as soon as the patient receives iron.

Since removal of hookworms leads to a fall in reticulocytes, and since the oxidation of tyrosine is involved in the maturation of reticulocytes (Gad et al. 1944) just as it is necessary for the production of melanin in the skin, the question arises whether reticulocytosis and the coctic blood picture as a whole are due entirely to the hyperactivity of a bone-marrow stimulated by peripheral blood-loss or partially to an inhibition by parasites of tyrosine oxidation.

If a half-saturated solution of *p*-aminobenzoic acid is neutralised with solid sodium bicarbonate and injected into the depigmented skin of an untreated African anæmia, a dark patch will develop within 6–12 hours, reaching its deepest colour within a day. Injection of a tyrosine suspension into the same pale skin will be followed by the appearance of a dark patch only after several days. If the same tyrosine suspension is injected a day after removal of hookworms, the dark patch will start appearing within a few hours and reach its maximal colour depth within a day. Here again the results are more striking if the iron-deficiency part of the anæmia has been corrected previously.

DISCUSSION

In an intensive investigation of adult patients at Mulago hospital, which will be published elsewhere, it was found that various specific symptoms of kwashiorkor as described from Uganda, such as liver damage (Davies 1948, Holmes and Trowell 1948), pancreas insufficiency (Davies 1948), renal failure (Hennessey 1938), skin colour changes, straight hair, swollen parotid glands, and sexual immaturity (Trowell 1944, Trowell and Muwazi 1945, Trowell 1947), were not necessarily seen together. The only common findings were always anæmia and hookworms or other parasites, which were associated with one or more of the kwashiorkor symptoms.

Skin and hair changes when found with ancylostomiasis can be reversed by worming; one might speculate whether the various lesions in parenchymatous organs,

TABLE V—DIFFERENCE IN RECOVERY PATTERN FROM IRON-DEFICIENCY ANÆMIA ON IRON TREATMENT, BETWEEN PATIENTS FIRST TREATED FOR ANCYLOSTOMIASIS AND OTHERS NOT SO TREATED. (ONLY CASES NOT COMPLICATED ON ADMISSION OR DURING RECOVERY BY MALARIA OR BACTERIAL INFECTION HAVE BEEN INCLUDED)

Patients	Maximal reticulocyte-count (%)				
	2–10	11–20	21–30	31–40	41–50
5 patients first wormed	4	1	..	..	..
12 patients not wormed	1	5	3	2	1
	Maximal M.C.V. rise (c. μ)				
	0–10	11–20	21–30	31–40	41–50
5 patients first wormed	3	2	..	..	..
12 patients not wormed	0	4	3	3	2

TABLE IV—CASES OF SEVERE HOOKWORM ANÆMIA ADMITTED TO HOSPITAL WITHOUT IRON DEFICIENCY BUT WITH MALARIA OR SUBCLINICAL BACTERIAL INFECTION

Findings and course	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Hæmoglobin (g. per 100 ml.)	4·29	3·05	4·23	3·62	3·41	4·72
Reticulocytes (%) ..	..	..	12·0	12·2	3·2	2·6
M.C.V. (c.μ) ..	106·0	127·0	135·5	131·5	99·2	98·6
M.C.H. (μμg.) ..	30·6	37·0	38·5	39·3	29·4	28·9
M.C.H.C. (%) ..	28·8	30·4	28·4	29·9	29·8	29·3
Complications ..	Splenomegaly; bacterial infection	Pregnancy; malaria	Bacterial infection	Pregnancy; malaria	Bacterial infection	Bacterial infection
Outcome	Death due to sepsis (Friedländer's bacillus)	Left hospital on day of admission	Response to penicillin and worming	Response to mepacrine and worming	Death from pneumonia	At first, response to penicillin and worming; later, death from pneumonia

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TABLE VI—RESPONSE OF HYPOCHROMIC ANÆMIA TO ANTHELMINTIC TREATMENT, AT FIRST WITHOUT IRON MEDICATION

Blood findings	Admission	4th day	8th day		15th day	22nd day		29th day		32nd day	36th day	43rd day	50th day
Hb (g. per 100 ml.)	4·20	3·91	3·48	*1st worming*: removal of 824 *Necator americanus* and 2 *Hymenolepis nana*	4·21	4·63	*2nd worming*: removal of 6 *N. americanus*	4·85	Start of Fe therapy	6·08	7·25	9·46	10·71
Red cells (per c.mm.)	1,602,500	1,485,000	1,575,000		1,681,600	1,952,500		2,098,750		2,142,000	2,528,250	3,270,000	3,680,000
Reticulocytes (%)	4·5	6·8	5·0		5·6	0·9		2·8		2·1	4·8	1·6	0·4
Cell volume (%)	14·7	14·0	13·7		15·0	17·1		18·0		21·5	26·3	32·0	34·5
M.C.V. (c.μ)	91·7	94·4	87·0		89·2	87·4		85·8		100·0	103·5	97·8	93·8
M.C.H. (μμg.)	26·2	26·3	22·1		25·0	23·7		23·1		28·3	28·6	29·3	29·2
M.C.H.C. (%)	28·6	27·9	25·4		28·0	27·0		26·9		28·3	27·5	29·6	31·1
Blood volume (ml.)	4830	..	4780		5020	5120		5000		..	4940	..	5560
Total circulating hæmoglobin (g.)	203	..	167		211	237		243		..	358	..	596

such as liver, kidney, and pancreas, could be explained to some extent by parasites and anoxæmia acting on tissues poorly nourished and highly dependent on oxygen.

Smillie's (1928) description of the symptoms of ancylostomiasis reads remarkably like one of kwashiorkor. Williams (1940) found, in children, skin and hair changes caused by ascariasis, and Hennessey (1938) considered bacterial infection rather than malnutrition to be the cause of the kidney changes observed by him in Uganda. Gelfand (personal communication) has expressed doubt whether malnutrition is the fundamental cause of kwashiorkor.

It would be unwise to belittle the need for an improvement in nutrition in Central Africa. In Uganda most women consider eggs as taboo. Milk and meat are expensive in a country where the tsetse fly is endemic. Thus it is difficult for infants to obtain a diet containing sufficient protein and easily digestible unless they are suckled up to the age of 2 years. However, if anæmia and parasites play an important part in the causation of kwashiorkor of adults, and if the main causes of anæmia are helmintic infestation and malaria and bacterial infections, the prevention of kwashiorkor must be looked for not only in dietary improvements but also in fields hitherto often insufficiently considered. It will become necessary to distinguish between nutritional upset caused by parasites and malnutrition due to faulty diet. While the first will be more severe in people who are poorly fed, unlike true malnutrition it will not be cured by dietary measures alone.

SUMMARY

In 44 patients with severe anæmia studied in Central Africa, the cause of the anæmia was always peripheral blood-loss. In 32 patients the blood-loss was extravascular and due to hookworms. These patients had an iron-deficiency anæmia. In 6 patients the hookworm anæmia was complicated on admission by malaria or bacterial infection. The remaining 6 patients had either malarial anæmia or anæmia of infection. The blood-loss being intravascular in these latter patients, no iron deficiency was noted on admission.

The macrocytes in Central African anæmia are reticulocytes and young cells in general, emitted by an efficiently functioning bone-marrow into a periphery where constant blood-loss occurs.

The macrocytes as seen in Central Africa are described as "coctic," and differences from the megalocytes of the nutritional macrocytic anæmia of Wills are pointed out.

The pattern of response to iron treatment of hypochromic anæmia is different in African patients from that seen in Europe.

Iron alone will not fully cure patients with hypochromic anæmia, though it may restore a normochromic blood picture. Full recovery will take place after the removal of hookworms. Patients can have hookworm anæmia without a deficiency of iron. On the other hand, evidence is adduced to show that the iron-deficiency anæmia is caused by ancylostomiasis.

The removal of hookworms leads to darkening of the skin in patients whose iron deficiency has been corrected. It also causes the disappearance of other kwashiorkor symptoms. The possibility is discussed of inhibition by parasites of tyrosine oxidation being the cause of both the pale skin and, at least partially, the escape of coctic cells into the blood-stream. Tests in which tyrosine is injected into the skin are described to support the first part of this theory.

It is emphasised that the extermination of parasites will have to be an essential measure in the prevention of kwashiorkor.

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STREPTOMYCIN IN HUMAN PLAGUE

COMPARED WITH OTHER TREATMENTS

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IN a preliminary communication[1] in January, 1948, we gave a brief account of the successful use of streptomycin in the outbreak of plague in the Anantapur district of Madras. Here we propose to analyse 206 cases in that outbreak and to compare the effect of the various treatments tried.

CLINICAL VARIETIES

Bubonic Type (85% of cases).—In most cases the buboes were in the femoral region. Next in frequency came the axillary buboes, then the inguinal, and finally the cervical. Submental, supraclavicular, submandibular, popliteal, and posterior auricular buboes were also seen. The femoral buboes usually subsided without suppurating, whereas the inguinal buboes commonly suppurated and had to be incised. The axillary buboes ran a protracted course with severe periadenitis and often cellulitis of the surrounding areas, accompanied by intense toxæmia. This was the most dangerous type. Buboes situated in other uncommon places rarely suppurated. Multiple buboes were met with in 2% of cases.

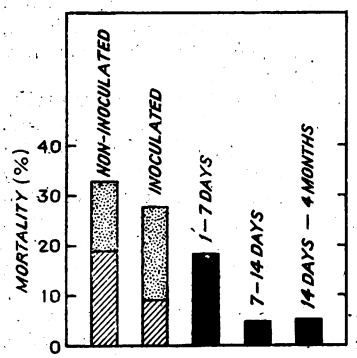

Fig. 1—Case-mortality of plague among 120 inoculated and 86 non-inoculated patients; hatched areas, patients admitted moribund; black columns, case-mortality in relation to time of inoculation before onset.

Septicæmic Type (8% of cases).—In this type the temperature was very high from the onset, with intense toxæmia. The tendency to subcutaneous hæmorrhage was great. When subcutaneous or intramuscular injections were given, there was a sudden spurting of blood the moment the needle was removed, but it stopped within a few seconds.

Cellulocutaneous Type (4% of cases).—This was an invariably fatal type. The patient was prostrated and highly toxic from the very start of illness. The temperature often ranged between 99 and 101°F, indicating poor resistance. The most common site of the lesions was the pectoral region, where there was diffuse swelling and acute tenderness of the skin and subcutaneous tissues. Death was sudden within twenty-four hours of onset from heart-failure supervening on toxic myocarditis.

Intestinal Type (3 cases).—These patients had vomiting and bloody diarrhœa. The stools were large and frequent and contained 1–2 oz. of blood; but this lasted only twenty-four hours.

Cerebral Type (1 case).—The temperature on the first day of fever was 105°F, and the patient was semiconscious and highly toxic. Next day he became fully unconscious and violent. Involuntary movement of the head was the first sign noted. Twitchings of the neck muscles and later of the hand muscles developed. Breathing became shallow, and the patient died in two hours.

Pneumonic Type (2 cases).—One of the patients in this group showed signs of early consolidation and had a protracted course, but ultimately recovered; the other was a doubtful case, which showed pneumonic signs at the time of death.

MORTALITY

The total mortality in our series was 29·5%, of which 13·8% was made up of cases moribund on admission. This high mortality is due to the fact that almost all the patients, especially those coming from the rural areas, had a long way to come and were in a late stage on admission, usually after the third day of fever. The main reasons for this were lack of transport and the reluctance of illiterates to report cases of plague.

Value of Inoculation.—Among 120 inoculated patients the mortality was 27·5%, including 9·1% moribund on admission, and among 86 who had not been inoculated it was 32·5%, including 18·6% moribund on admission (fig. 1). This shows that inoculation did not give protection, though perhaps it gave a slightly better chance of survival. The mortality among inoculated patients was composed of 18% among those who had been inoculated 1–7 days, 4·5% among those inoculated 7–14 days, and 5% among those inoculated from 14 days to 4 months before the onset of plague (fig. 1). This seems to show that immunity develops a week or so after inoculation. We could not assess the value of inoculation after a longer period than 4 months, because the epidemic did not last long.

Relation to Onset of Fever.—Our case-records show that most of the deaths took place on the third, fourth, or fifth day of fever. If a patient survived the fifth day of fever, prognosis was good. Such deaths were usually due to heart-failure. Late deaths—i.e., those which took place a week or more after the onset of fever—were mostly complicated by dehydration consequent on diarrhœa, pneumonia, or bronchopneumonia.

TREATMENT

Sulphathiazole and Sulphadiazine.—Sulphadiazine gave better results than sulphathiazole. It was less toxic and was well tolerated. Children tolerated the drug much better than did adults. Children aged 5–6 years were given 3 g. a day without developing any toxic symptoms. The routine treatment was as follows:

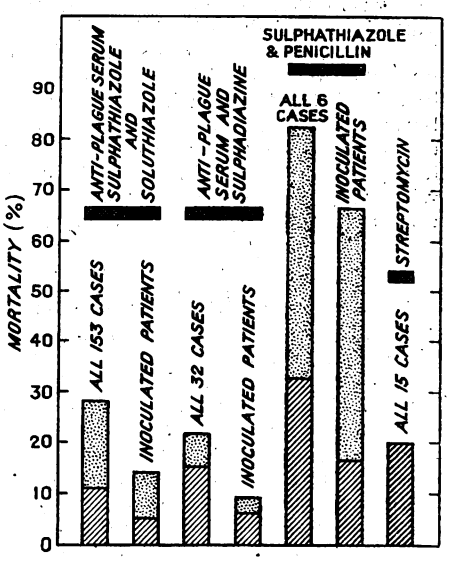

Fig. 2—Case-mortality of plague under different treatments; hatched areas, patients admitted moribund.

As soon as a patient was admitted a mixture containing 10 ml. of 25% sodium sulphadiazine, 10 ml. of 25% glucose, and 300 mg. of 'Celin' in 40 ml. of distilled water was given intravenously. Immediately after the injection 2 g. of sulphadiazine was given by mouth, followed by 1 g. four-hourly until the temperature fell to 100°F. Then 1 g. was given eight-hourly until the temperature became normal. In addition vitamin B_1 10 mg. b.d. and nicotinic acid 75 mg. t.i.d. were given. In successful cases the toxæmia disappeared within forty-eight hours, and the temperature fell to normal in four days.

1. Karamchandani, P. V., Rao, K. S. *Lancet*, 1948, i, 22.

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Anti-plague Serum.—The judicious use of curative anti-plague serum is often beneficial in unprotected cases and cases with a high initial temperature and toxæmia. The serum should be given early in the disease and in sufficient quantity—at least 60 ml. It should be continued for at least three days. Sulphonamide-resistant cases were observed to respond to this serum. The addition of 0·5 ml. of 1 : 1000 adrenaline hydrochloride to the serum prevents serum-sickness. No case was treated with serum alone.

Penicillin was tried in 6 cases. Penicillin 40,000 units was given on admission, followed by 20,000 units three-hourly. It had no action whatever on plague. The temperature did not fall, nor was toxæmia reduced. Penicillin was therefore abandoned.

Streptomycin.—If there is any specific against plague it is streptomycin. All 15 patients selected for treatment with this drug were apparently moribund with hyperpyrexia, intense myocarditis, extreme general toxæmia, and a fast feeble running pulse due to heart-failure supervening on toxic myocarditis.

The 3 patients who died did so within a few hours of admission, and all 3 were admitted after the third day of fever, with a low temperature following hyperpyrexia, indicating impending dissolution consequent on exhausted bodily resistance and no leucocytosis. In discussing the comparative mortalities in the different treatments (fig. 2) it must be kept in mind that streptomycin was given only to patients admitted apparently moribund or to patients who had become apparently moribund after admission, not having responded to sulphadiazine. Therefore, though fig. 2 shows similar mortalities for streptomycin and for sulphadiazine, there is this vital difference that streptomycin saved 3 patients who, in all probability, would have died under sulphadiazine therapy.

The success which crowned streptomycin therapy even in patients who had become apparently moribund under treatment with sulphadiazine led us to try streptomycin in worse and still worse cases, till we found its limit of usefulness. Though this limit has been reached, it does not detract from the brilliant success of streptomycin therapy, under which no patient died who was not already moribund when the treatment was started. We have since found that a total of 1–2 g. of streptomycin is the minimum effective dosage, while the maximum is 8 g. spread over 4 days, with individual doses of 0·5 g. every six hours.

It is our view that bubonic and septicæmic types of plague will quickly respond to streptomycin. It would be profitable to combat initial toxæmia with anti-plague serum.

SUMMARY

Of the 206 cases of plague in Anantapur District of Madras Presidency analysed, 85% were of bubonic type, 8% septicæmic, and 4% cellulocutaneous; 3 cases of intestinal, 2 of pneumonic, and 1 of cerebral type were also encountered.

The mortalities under different treatments are given. Though the mortality under streptomycin therapy was 20%, compared with 22% for sulphadiazine, 3 patients who became apparently moribund under sulphadiazine treatment were saved by streptomycin.

Under streptomycin therapy 3 patients died, but they were moribund on admission and died before receiving 1 g. of streptomycin, which is considered to be the minimum total dosage needed to cure plague. Streptomycin therapy seemed to be superior to any other treatment.

The total mortality was 29·5%, of which 13·8% was made up of patients moribund on admission.

The mortality among inoculated patients was 27·5% and among uninoculated 32·5%.

EXPERIMENTAL PANCREATICOGASTROSTOMY*

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RADICAL pancreaticoduodenectomy has become established during the last ten years as a sound operation for ampullary carcinoma, for carcinoma of the common duct, and to a lesser extent for carcinoma of the head of the pancreas. From published reports it appears that opinion is divided as to whether a single-stage operation is to be preferred to a two-stage operation. We agree with the majority that the single-stage operation is preferable and that it is tolerated better than one would expect. We believe also that it is safer to implant the common duct into the jejunum than to tie it off, and perform cholecystgastrostomy, because of the risk of breakdown and leakage. Finally, it seems preferable to implant into the alimentary canal the remaining pancreas after excision of the head, because of the dangers of pancreatic fistula and nutritional disturbance.

The degree of nutritional disturbance suffered after exclusion of pancreatic juice from the gut varies in different patients, and its incidence and severity are unpredictable before operation. It seems to be the general judgment that these disturbances are sufficiently common and incapacitating to warrant reimplantation of the remaining pancreas.

There are many minor modifications of the Whipple operation, but in all cases the pancreas is implanted either into a unilaterally excluded loop of small intestine, by inserting it higher than the gastro-enterostomy, or into a loop whose two arms are united by an entero-enterostomy.

Experience has shown that gastrojejunostomy and choledochojejunostomy are safe procedures, and that ascending infection along the common bile-duct is less common after choledochojejunostomy than after cholecystogastrostomy. Of all these steps, it is the pancreatic implantation into the jejunum that gives cause for anxiety.

The professorial unit in the Department of Surgery of Liverpool University has had experience of only five cases of pancreatic excision for carcinoma, but that experience has been instructive.

In case 1, a married woman aged 45, the operation was done in two stages, of which the first was a cholecystogastrostomy. At the second operation the duodeno-pancreatectomy was performed and the remaining pancreas was cut across and oversewn. Convalescence was uneventful, and there was no subsequent nutritional disturbance. In particular, there was no demonstrable excess of unsplit fat in the stools. The patient died of recurrence 18 months after operation.

In case 2, a married woman aged 53, a two-stage operation was again undertaken; but, in addition to the implantation of the gall-bladder, the stomach was divided and a gastrojejunostomy performed at the first session. This shortened the second stage but made it very difficult because of adhesions. In preference to tying it off, the common duct was implanted into the jejunum and the stump of the pancreas oversewn. Convalescence was stormy and the postoperative period characterised by intermittent fever and dyspepsia. The patient died in a febrile crisis 8 months after operation.

In case 3, a man aged 50, the same procedure was followed as in case 2. Ten days after the second operation the pancreatic stump broke down and an external fistula developed. This became uncontrollable when the pancreatic leak was augmented by leakage of bile. The patient died in dehydration a month after his operation.

* A shorter version of this paper was read by one of us (D. A.) before the Association of Surgeons in Edinburgh in May, 1948.

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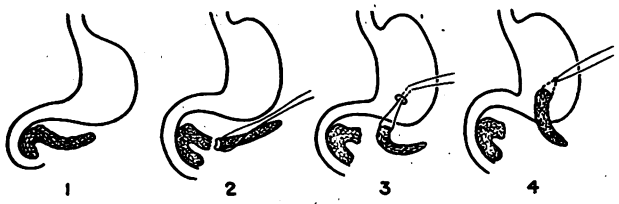

Fig. 1—Implantation of pancreatic tail into stomach in dog.

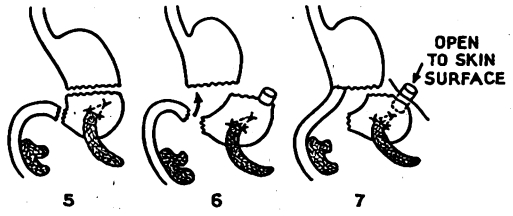

Fig. 2—Formation of pyloric pouch, closed except to surface, into which pancreatic tail had previously been implanted.

In cases 4 and 5, men aged 75 and 54, a different procedure was followed. Despite the patients' indifferent general condition the operations were successfully completed in one stage. In each case the common duct and the pancreas were implanted into the jejunum proximal to the gastro-jejunal anastomosis. In case 4 a small catheter was tied into the pancreatic duct and an end-to-side pancreatico-jejunostomy was made. In case 5 the pancreatic stump was intussuscepted into the end of the jejunum with great care and thoroughness. The sequel was identical in the two cases. Good progress was made for a week. Then the patients' general condition deteriorated sharply, with abdominal pain. An external pancreatic fistula developed rapidly, and death took place on the 9th and 10th postoperative days.

These experiences led us to the conclusions we have stated. Thus we favour an operation completed in one stage, with implantation of the common duct into the jejunum. We believe that division of the pancreas, with careful closure of the residual tail or body, is the safer procedure, but that, taking the long view, implantation of the residual pancreas into the alimentary tract should be the aim of operators in this field.

In our two cases of pancreatic implantation, necropsy revealed separation of the pancreas from the jejunum, with localised fat-necrosis and all the signs of acute pancreatitis in the part of the organ nearest to the small intestine. Physiologically, it seems optimistic to expect successful implantation of the pancreas into the jejunum in which is produced the enterokinase required to convert trypsinogen into trypsin and in which the pH is optimal for tryptic action, with resulting digestion at the anastomosis. We decided therefore to observe in dogs the effect of implanting the tail of the pancreas into the stomach. Later we found that these experiments were similar in object and differed only in detail from the work of Tripodi and Sherwin [1] and of Person and Glenn.[2] Indeed, our results simply confirm their findings.

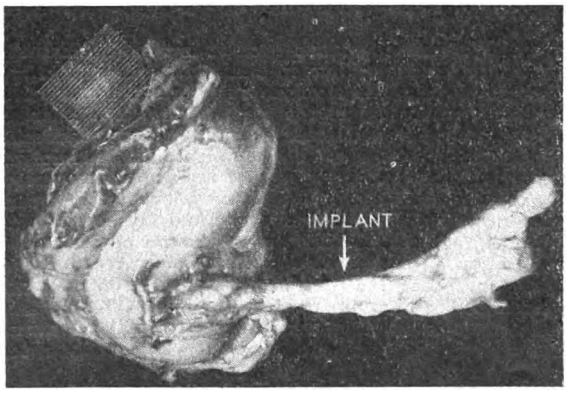

Fig. 3—Pyloric pouch with implanted pancreas removed on 66th day.

PROCEDURE

In seven dogs we implanted the tail of the pancreas into the stomach. In one we placed it in the fundus; this dog died of acute hæmorrhagic pancreatitis, and at necropsy we found massive œdematous swelling of the pancreatic implant, with hæmorrhagic peritoneal exudation and subperitoneal hæmorrhages. In the remaining six dogs we implanted the tail of the pancreas into the pyloric end of the stomach.

Technique.—Under general anæsthesia the pancreas was divided about the junction of the head with the tail, leaving about 2½–3 in. of the tail. The resulting cut surface at the head was simply oversewn. The tail of the pancreas, with its blood-supply intact, was mobilised and brought to the stomach, and a 'Nylon' suture was passed through its thickness near the cut end. An opening was made into the anterior surface of the stomach near the pylorus, sufficient to admit the cut end of the tail of the pancreas. The nylon suture was threaded on a needle, passed through this opening, and brought out through the anterior wall of the stomach again. Traction was applied to this suture so as to draw in half an inch of the pancreatic tail, and the suture was tied (fig. 1). Omentum was lightly fixed about the anastomosis. This procedure was carried out in six dogs. All the dogs recovered from the operation, were taking fluids within 24 hours and were eating a normal diet of biscuits and meat by the 5th day.

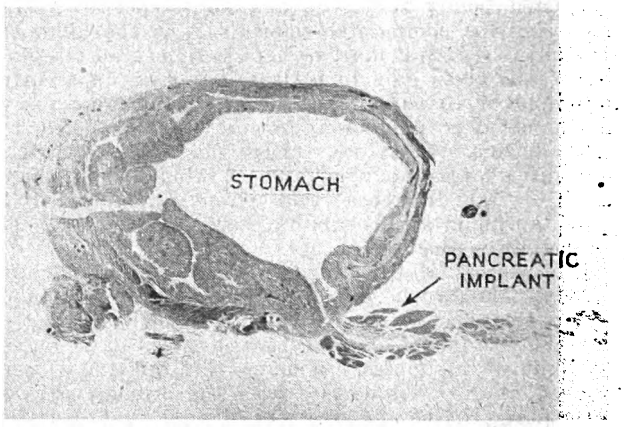

Fig. 4—Section through pancreatic implant into stomach, showing pancreatic duct patent and opening into stomach lumen in dog killed on 66th day.

RESULTS

To observe the implant on the 15th postoperative day, one dog, though perfectly well, was killed. Examination of the site of implant showed normal uninflamed pancreas firmly held in the stomach wall. The redundant part of the pancreas within the lumen of the stomach had been digested to the level of the gastric mucosa. Histological examination showed firm union and digestion down to the mucosal level. The 3 inches of the pancreatic tail outside the stomach appeared normal.

Five dogs remained. One of these died on the 51st postoperative day, having progressively lost weight and become grossly anæmic. Necropsy revealed general wasting, with fatty infiltration of the liver, and a bone-marrow with no signs of hæmopoiesis. The implant,

1. Tripodi, A. M., Sherwin, C. F. *Arch. Surg.* 1934, 28, 345.
2. Person, E. C. jun., Glenn, F. *Ibid*, 1939, 39, 530.

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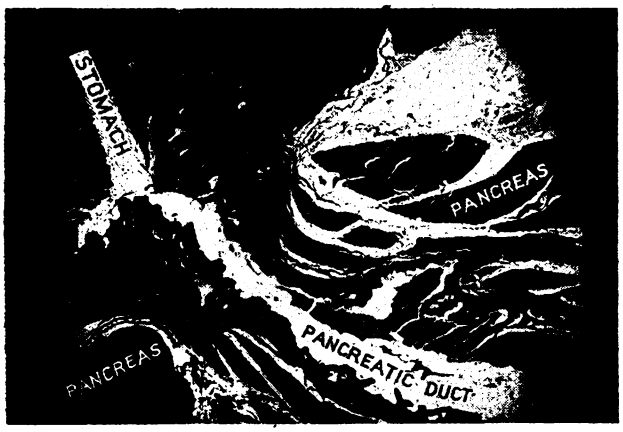

Fig. 5—Anastomosis between stomach and pancreatic duct, showing fusion of mucosæ (same section as in fig. 4, under higher power).

however, was satisfactory, being uninflamed and showing no signs of earlier leakage. There was slight pancreatic atrophy. That this dog did not die of pancreatic insufficiency is certain, because the major part of the pancreas, the head and body, was intact, of normal appearance, and in functional continuity with the alimentary tract.

Four dogs remained in a state of excellent health and nutrition. A second operation to collect pancreatic juice produced by the implant was performed at intervals of 40–60 days from the first. A pouch with blood-supply intact, closed save for an opening to the skin surface, was made from the pyloric end of the stomach in which the tail of the pancreas had previously been implanted. The continuity of the gastro-intestinal tract was restored by gastroduodenal anastomosis (fig. 2).

After 45, 45, 49, and 66 days from the original implant the dogs were anæsthetised, the splanchnic nerves were divided, and secretin was injected intravenously. Pancreatic juice then accumulated in the pouch. In all four dogs amylase was demonstrated in convincing quantity by the digestion of starch. The secretion of the dog's stomach contains no amylase, which can therefore be presumed to have come from the pancreatic implant.

These experiments having been performed, the pyloric pouch with the implant intact was removed (fig. 3). In two of these specimens the pancreas was of normal macroscopical appearance, whereas in the other two there was some atrophy. In the specimen removed 66 days after the original implantation a section (figs. 4 and 5) showed clearly the complete continuity between the pancreatic duct and the lumen of the stomach. Microscopy showed that the gastric mucosa had fused with that of the pancreatic duct, there being a gradual and continuous change from one to the other. The pancreatic glandular tissue was identical histologically with that of the normal pancreas; there was no evidence of inflammation, and there was firm union at the site of anastomosis.

CONCLUSIONS

It seems certain that the tail of the pancreas can safely be implanted into the stomach in dogs and that secretion will continue. In considering the clinical application of this experimental work it should be borne in mind: (1) that the pancreas has a complete peritoneal covering in the dog, whereas in man it is deficient posteriorly (Person and Glenn,[2] recognising this fact, stripped the peritoneal covering from the pancreas before implanting it); and (2) that the pancreas in the dog is freely mobile, whereas in man it is fixed to the posterior abdominal wall.

We have performed pancreaticoduodenectomy with implantation of the pancreatic tail into the stomach in the cadaver where it presents no difficulty. By mobilising $1^1/_2$–2 in. of the remaining pancreas at the point of division it is easy to turn it forward and implant it through the posterior wall of the pyloric end of the stomach, the two being in direct apposition. We have no knowledge of the procedure having been used in man in the operation of pancreaticoduodenectomy, where it appears to offer some hope of overcoming the dangers attendant on the more usual procedure of implantation into the jejunum.

SUMMARY

Of six dogs in which the pancreatic tail was implanted into the stomach five remained well until killed on the 15th, 45th, 45th, 49th, and 66th days.

In all six dogs the implant was intact and showed no signs of leakage or inflammation.

In all four dogs tested, amylase was produced by the pancreatic implant.

In three specimens the pancreas appeared macroscopically normal, and in three there was some pancreatic atrophy.

Histological section showed without doubt the success of the anastomosis in the dog killed on the 66th day.

We wish to thank Prof. R. A. Gregory for his invaluable help and advice.

PENICILLIN AND CARONAMIDE IN RESISTANT SUBACUTE BACTERIAL ENDOCARDITIS

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EFFECTIVE inhibition of the excretion of penicillin, to promote a higher serum-penicillin level than that normally obtained, has become possible through the use of 'Caronamide' (4'carboxyphenylmethane-sulphonanilide). Beyer et al. (1947) found that this compound can block the excretion of penicillin without damaging the kidneys. The fact that serum-penicillin levels are higher than usual during combined therapy with oral caronamide and parenteral or oral penicillin, as reported by these workers, was confirmed by Hunter and Wilson (1948), who also commented on the lack of toxicity of caronamide in the dosage used. Seeler et al. (1948) estimated that the effect of caronamide in prolonging plasma-penicillin levels was greater than that resulting from a tenfold increase in penicillin dosage.

We report here the successful use of combined penicillin and caronamide therapy in two cases of subacute bacterial endocarditis which had relapsed after repeated courses of penicillin alone. In a third patient a brief course of caronamide during penicillin therapy for bacterial endocarditis caused clinical improvement, which had not occurred with penicillin alone. Toxic effects probably due to the caronamide were observed in the first two patients. The serum-penicillin levels during therapy with penicillin alone and during combined therapy were recorded in cases 1 and 2 by one of us (J. C.). Serial dilutions of serum in phenol-red glucose serum-water medium (May et al. 1947) were inoculated with a culture of the Oxford staphylococcus and compared with similarly inoculated dilutions of penicillin in the same medium. Sensitivity to penicillin of the organisms recovered from

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the same patients was tested by comparison with the Oxford staphylococcus in the above-mentioned medium containing dilutions of penicillin.

Case 1.—A man, aged 28, with a previous history of heart disease following three attacks of rheumatic fever, came under observation in January, 1947, with painful swellings on fingers and forearms. He had mitral stenosis and aortic incompetence. Fever, tachycardia, subungual hæmorrhages, an enlarged spleen, and leucocytosis were present, but a blood-culture was sterile on each of four occasions. Penicillin totalling 13·5 mega units given for 28 days controlled the fever and symptoms, but pains in the fingers and toes returned in June, 2 months after the end of treatment. Blood-culture was now positive, and the organism (*Strep. viridans*) was sensitive to between 0·03 and 0·015 unit/ml. of penicillin. A second course of penicillin, lasting 43 days and totalling 53·5 mega units, again controlled fever and symptoms, and the blood-culture was sterile 19 days after the end of treatment. A relapse 2 weeks after discharge led to a third course of penicillin, totalling 143 mega units and lasting 3 months. *Strep. viridans*, recovered from the blood before treatment, was still sensitive to between 0·03 and 0·015 unit/ml. of penicillin. The patient relapsed 2 weeks after the cessation of penicillin therapy, though his general condition was good. Blood-culture was again positive in February, 1948, the streptococcus being again sensitive to 0·03 unit/ml. of penicillin and also to 0·25 μg/ml. of streptomycin. A course of intramuscular streptomycin lasting 23 days and totalling 72·5 g. was given, but though fever was at first controlled it later returned, and positive blood-cultures were obtained immediately after the end of the course. The streptococcus had now become more resistant to streptomycin but was still inhibited by 0·125 unit/ml. of penicillin.

At the start of the fourth course of penicillin in April, 1948, the man's clinical state had altered only slightly. Fever, tachycardia, and embolic phenomena were still present, and his urine contained occasional red cells. Penicillin was given intramuscularly at the rate of 300,000 units 3-hourly for 9 days, during which the serum-penicillin levels were estimated. Caronamide 4 g. 4-hourly was given by mouth in addition on the 9th day, and combined therapy was continued for 30 days. Fever was controlled even before the caronamide was begun, but occasional embolic phenomena developed during the first 3 weeks of combined therapy. Nausea followed the administration of caronamide but was eased by previous administration of phenobarbitone. Œdema of the lumbar region was observed on the 26th day of combined therapy and persisted for about 10 days. Six successive daily blood-cultures taken after the end of therapy were sterile.

The patient remained clinically well during the following 5 months. The signs of mitral stenosis and aortic incompetence continued, but clubbing of the fingers slowly disappeared. Blood-cultures were sterile on three occasions. Fig. 1 shows the serum-penicillin levels, during therapy with penicillin 300,000 units 3-hourly, before and during caronamide therapy.

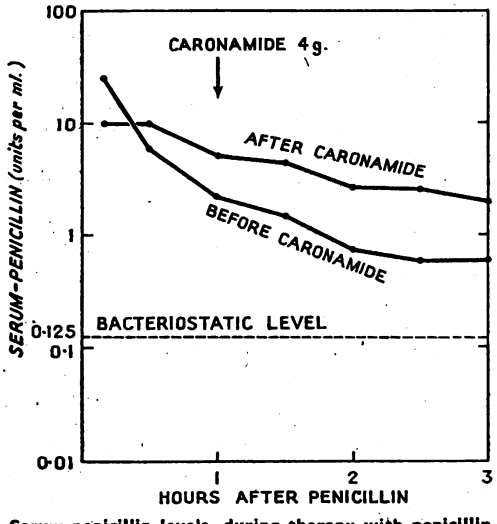

Fig. 1—Serum-penicillin levels, during therapy with penicillin 300,000 units 3-hourly, before and during caronamide therapy (case 1). Each graph is average of three estimations.

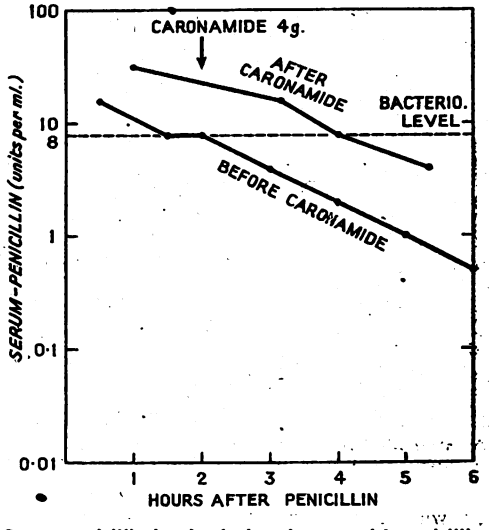

Fig. 2—Serum-penicillin levels, during therapy with penicillin 1 mega unit 6-hourly, before and during caronamide therapy (case 2).

Case 2.—A woman, aged 34, without any history of previous heart disease or rheumatism, developed fever and painful swellings in the calves, thighs, and fingers in February, 1947. On her first admission in April, 1947, intermittent irregular pyrexia, subungual hæmorrhages, Osler's nodes, and an apical systolic murmur were noted, but the heart was not enlarged. Blood-culture was positive, and the organism (*Strep. viridans*) was relatively resistant to penicillin but was inhibited by concentrations in excess of 4 units per ml. A course of penicillin of varying dosage and totalling 140 mega units, given between April and July, controlled the symptoms and fever. A short second course of penicillin was given in August during dental extraction, but blood-cultures were again positive before and after this course. The streptococcus exhibited the same degree of resistance to penicillin and was sensitive to 1·5 μg/ml. of streptomycin. A third course of penicillin, totalling 28 mega units, and a course of streptomycin totalling 34·5 g., both failed to sterilise the blood; and, though the patient's general condition remained good, irregular fever and embolic phenomena continued.

In May, 1948, the streptococcus obtained by blood-culture was sensitive to a minimum of 8 units/ml. of penicillin and 32 μg/ml. of streptomycin. There was no fever, but embolic phenomena were present in the hands and feet. The cardiac condition was unchanged. The urine was normal. Intramuscular penicillin was begun at the rate of 4 mega units daily in divided doses of 1 mega unit 6-hourly, and after 9 days caronamide 4 g. was given by mouth 4-hourly in addition. Nausea was experienced but was not troublesome. On the 16th day of treatment penicillin was increased to 1 mega unit six times daily. On the 18th day, when caronamide had been given for 9 days, fever, aching pains, and malaise began. On the 21st day fever persisted, the leucocyte-count had fallen to 3000 per c.mm., and caronamide therapy was therefore suspended, penicillin being continued for a further 6 days. Slight œdema of the skin of the back was noted at this time. During the next few days improvement set in, the temperature became normal, and the leucocyte-count rose slightly. Three successive daily blood-cultures were sterile a week after the end of penicillin treatment.

The patient remained well during the succeeding four months, and blood-culture, five months after the end of therapy, was sterile. Fig. 2 shows the serum-penicillin levels, during treatment with penicillin 1 mega unit 6-hourly, before and during caronamide therapy.

Case 3.—A girl, aged 18, with a history of rheumatic fever at the age of 3 years, and known to have had mitral stenosis since the age of 8 years, came under observation in January, 1948, with a swollen right ankle and was admitted on Feb. 23 to the orthopædic department at the Grimsby General Hospital. Her left ankle, left shoulder, elbows, and smaller joints then became swollen. Temperature 100·2°F. Cardiac enlargement slight but definite with systolic and late diastolic

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bruits at the apex. Erythrocyte-sedimentation rate (E.S.R.) 46 mm. in 1st hr. (Westergren) on March 5. Urine contained a trace of albumin; but no blood or organisms. Full dosage with salicylates produced no remission of temperature, which continued to rise in the evenings, but there was some diminution of pain and swelling in the joints. On March 12 calcium aspirin was substituted for salicylates with no subsequent benefit. On March 18 a parasternal diastolic murmur was first audible. The white-cell count on March 19 was 17,000 per c.mm. (85% polymorphs); E.S.R. 55 mm. On March 26 Osler's nodes in finger-tips, splinter hæmorrhages, and a few scattered petechiæ were noted. The tip of the spleen was palpable. The urine contained no blood, a trace of albumin, and a few pus cells. On March 29 a blood-culture gave *Strep. viridans* sensitive to penicillin. Penicillin 1 mega unit daily in 3-hourly divided doses was continued until April 19. In this period a course of sulphadiazine was also given. There was no improvement as regards pyrexia, and petechiæ continued to appear. On April 19 caronamide 4 g. 4-hourly was given in addition to penicillin and continued for 3 days. The temperature then fell to normal. Because of nausea and lumbar discomfort the caronamide was then stopped, but the penicillin was continued for a further 14 days. There was no subsequent rise in temperature.

By June, when the patient was discharged, she had gained 14 lb. in weight. No further positive blood-cultures were obtained after caronamide therapy. In November, 1948, the patient remained well and was back at work despite her mitral stenosis.

DISCUSSION

Relatively few reports have been published about the treatment of penicillin-resistant cases of subacute bacterial endocarditis, though such cases have been recorded in most large series. Sodium *p*-aminohippurate, which is excreted by the renal tubules as well as by the glomeruli, was first suggested as capable of blocking the excretion of penicillin. It was used in a case of subacute bacterial endocarditis by Loewe et al. (1947), but disadvantages, such as the enormous intravenous dosage necessary and undesirable side-effects, attended its use. The same workers used caronamide as an adjunct to penicillin in nine cases of subacute bacterial endocarditis. The plasma-penicillin levels were raised, and toxic phenomena were not troublesome. The results of therapy were not reported. Boger et al. (1947) showed that a combination of penicillin and caronamide sterilised the blood in a case of subacute bacterial endocarditis which had not responded to repeated courses of penicillin and of streptomycin. Vander Veer and Richardson (1947) treated with combined penicillin and caronamide two cases of endocarditis which had relapsed "after previous insufficient treatment with penicillin"; one case did not respond, and the other developed a severe febrile reaction accompanied by a rash and anuria, for which reason the caronamide was stopped. McCoy and Meyer (1948) also treated with combined penicillin and caronamide two cases in which the organism isolated was moderately resistant to penicillin; in one case drug treatment was discontinued because of fever and a rash, while in the other a successful therapeutic result was obtained.

The cases reported by us indicate clearly that caronamide is an important adjuvant to penicillin therapy in subacute bacterial endocarditis resistant to penicillin alone. This effect appears to be due to the high serum-penicillin levels obtained in this combined therapy. Actual enhancement of the bacteriostatic activity of the penicillin by the caronamide seems unlikely, for caronamide has no inhibitory effect on bacteria. In a direct test of caronamide in vitro no inhibitory effect was observed on *Strep. viridans* recovered from case 2. Nor was the inhibitory effect of penicillin on this and other organisms enhanced by the presence of caronamide in the medium even in a concentration of 100 mg. per 100 ml.

The giving of caronamide for several days is not without unpleasant effect. All three of our patients complained of nausea, but suitable sedation overcame this. The fever and leucopenia observed in case 2 seemed to be a serious toxic effect, though a rash was not observed. Vander Veer and Richardson (1947) and McCoy and Meyer (1948) observed similar febrile reactions accompanied by a rash in one each of their patients. But the appearance of lumbar œdema in case 1 suggested that the caronamide was causing a temporary toxic effect on the renal function. Our patient had no impairment of urea clearance at this time, but Boger et al. (1947) found cells in the urine and a decrease in urea clearance in their patient. Since caronamide does not seem to be toxic to the kidney in healthy persons, possibly the already damaged kidney in subacute bacterial endocarditis may be more sensitive than the normal kidney to caronamide. Fortunately the effect appears to be temporary.

The present cases of subacute bacterial endocarditis throw some light on the factors involved in the failure of penicillin therapy in this disease. Resistance of the causal organism to the antibiotic, as in case 2, is clearly one reason for clinical resistance to therapy and yet cannot explain failure in case 1, in which the streptococcus was normally sensitive to penicillin in vitro. Streptomycin therapy likewise failed in each case in spite of an initial sensitivity of the streptococcus to streptomycin. These findings suggest that there are non-bacterial factors which affect the action of the antibiotic as in other types of infection (Davies et al. 1945). Possibly an excessively rapid excretion of penicillin or streptomycin prevents the attainment of the usual peak levels of the antibiotic shortly after injection, yet the serum-penicillin level in cases 1 and 2 before caronamide therapy did not seem to be abnormally low. Anatomical peculiarities in resistant cases may hinder the diffusion of penicillin into the endocardial vegetations. This may explain the failure in case 1. However, whether the cause is excessively rapid excretion or inaccessibility of the bacteria in the lesion, the maintenance of serum-penicillin levels higher than usual appears to aid chemotherapy.

SUMMARY

Three cases of penicillin-resistant subacute bacterial endocarditis were treated with intramuscular penicillin and caronamide by mouth.

Two of the patients had received numerous courses of penicillin and streptomycin therapy without control of their infection.

The combination of caronamide and penicillin controlled the infection in all three cases.

Caronamide therapy enhanced the serum-penicillin levels in two of the cases.

We are indebted to our colleagues Dr. T. E. Gumpert and Dr. H. P. Brody for permission to record cases 1 and 2 which were originally under their care. Part of the caronamide used in these cases was received as a gift from Messrs. Sharp and Dohme, to whom we extend thanks. The streptomycin was supplied by the Medical Research Council.

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RESISTANCE TO TUMOUR GROWTH IN RATS FED ON VITAMIN-B COMPLEX

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THE addition of vitamin-B complex to an ordinary mixed diet of hospital scraps had been shown to protect rats from many of the ill effects of exposure to gamma radiation,[1] so it seemed worth while to find out whether this addition of vitamin B would have any effect on a rat's susceptibility to implants of tumour grafts.

Black and white rats of a pure breed were used. These have been bred for over 25 years in the Barnato Joel Laboratories of the Middlesex Hospital, where most of these experiments were done. These stock rats are never mated to any rat, or to the offspring of any rat, which has ever been inoculated with any tumour graft, as it has been shown that acquired resistance to tumour growth is usually transmitted to the next generation.[2] The rats are normally fed on hospital scraps, which provide a good mixed diet on which they appear to flourish and keep free from disease.

The vitamin-B complex originally used was a yeast extract and aneurine crystals kindly given by Mr. F. A. Robinson, of Glaxo Research Laboratories.* The yeast extract contained riboflavine, nicotinic acid, pantothenic acid, biotine, and vitamin B_6. Fresh aneurine solution was made up every week. Later on, Glaxo Laboratories could not supply the yeast extract, so dry yeast, bran, and 'Marmite' were used instead, but it was impossible, when using this mixture, to standardise the quantity in the same way. There was no alteration in the aneurine used.

The Jensen's rat sarcoma used for these experiments normally doubles its volume in two or three days while the tumour is small; after a fortnight's growth or so the rate is often somewhat slowed down, particularly in small rats, where the tumour in its later stages represents a perceptible proportion of the rat's total weight (fig. 5*b*).

EXPERIMENTS

Group I

The first group of experiments was carried out on 31 young rats, which were given Glaxo yeast extract and aneurine all their lives; they were the offspring of rats fed on vitamin-B complex. The families of rats on this diet were usually inoculated with tumour when they were about three months old and weighed about 100 g., as normally rats appear to be very susceptible to grafts of Jensen's rat sarcoma at this age.

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2. Russ, S., Scott, G. M. *Proc. roy. Soc.* B. 1939, 128, 126.

* Enough aneurine and yeast extract was added to ensure that every rat had at least aneurine 15 µg., riboflavine 5 µg., pyrodoxine 10 µg., and pantothenic acid 100 µg. daily.

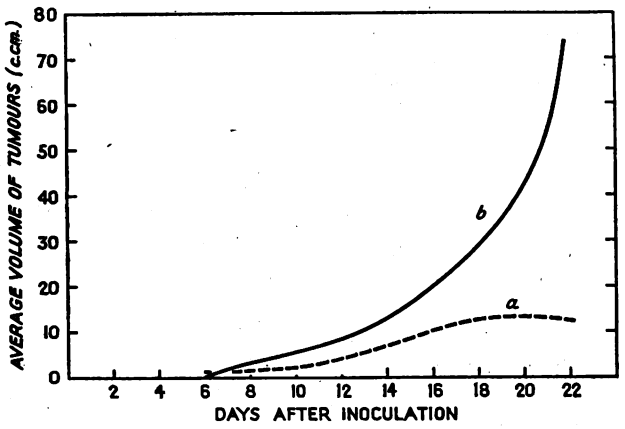

Fig. 1—Growth of tumours in (*a*) 31 rats (the offspring of parents fed on vitamin B) fed on Glaxo yeast extract and aneurine throughout their lives compared with that in controls (*b*).

These rats were matched in sex and weight with ordinary stock rats of the same breed, and inoculated in pairs (one rat fed on vitamin-B complex and one control) with small pieces of Jensen's rat sarcoma carefully matched under a magnifying glass to ensure that the pieces used for one couple were, as far as possible, of the same size and quality. In a few cases two controls were used. The grafts were planted in the flanks and measured twice a week. For the first one or two measurements the tumours in the rats fed on vitamin-B complex were often as large or even larger than those growing in the controls, but the rate of growth of the tumours in the rats fed on vitamin-B complex slowed down, while the control tumours forged ahead.

After about three weeks' growth, when many of the controls had to be killed owing to their very large tumours, the average volume of the tumours in the rats fed on vitamin-B complex was only a sixth of the average

	Days after inoculation							
	6	*10*	*12*	*14*	*16*	*18*	*20*	*22*
Average volume (c.cm.) of tumours:								
In 31 rats (offspring of parents fed on vitamin B) fed on Glaxo yeast extract and aneurine all their lives ..	0·7	2·6	4·05	6·6	9·8	11·9	13·0	12·5
In controls ..	0·6	5·3	8·25	14·9	20·1	28·6	40·3	73·0

volume of the tumours in the controls (fig. 1), and eventually 26 of the 31 tumours in the rats fed on vitamin-B complex disappeared.

Group II

The experiments in this group were done to see whether rats whose parents had been fed on normal diet could be made resistant to tumour growth if vitamin-B feeding

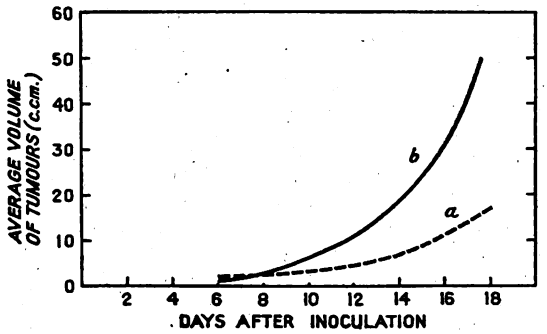

Fig. 2—Growth of tumours in (*a*) 27 rats (the offspring of parents on a normal diet) fed on Glaxo yeast extract and aneurine for 22-32 days before inoculation compared with that in controls (*b*).

began only a few weeks before inoculation of the tumour. Several families of young stock, 54 rats in all, were divided into two equal groups, half of each family being used as controls; one group was given the normal diet of hospital scraps, while the other had Glaxo yeast extract and aneurine added to their food. After vitamin-B complex had been given for at least three weeks (the actual time varied from twenty-two to thirty-two days), the two groups were inoculated with Jensen's rat sarcoma. Measurements showed that the average volume of tumours in the rats on vitamin-B complex, after eighteen days' growth, was less than a third of that in the controls (fig. 2):

	Days after inoculation					
	8	*10*	*12*	*14*	*16*	*18*
Average volume (c.cm.) of tumours:						
In 27 rats fed on Glaxo yeast extract and aneurine for 22–32 days before inoculation	2·2	2·25	3·75	5·5	11·0	16·0
In controls	3·4	6·5	11·2	22·2	29·4	55·5

Group III

The 18 rats used for this group of experiments were the offspring of parents on a normal diet, but the mothers were given extra vitamin-B complex from the day the

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young were born, and this feeding was kept up for the rest of their lives. The controls were normal rats of the same weight and sex. Dry yeast, bran, and marmite took the place of the Glaxo yeast extract. Twenty days after inoculation, the volume of the tumours growing in the rats on vitamin-B complex was only a sixth of that in the controls (fig. 3):

	Days after inoculation							
	6	8	10	12	14	16	18	20
Average volume (c.cm.) of tumours:								
In 18 rats fed on dried yeast, bran, marmite, and aneurine since birth ..	1·1	1·8	2·0	3·5	4·3	5·3	5·7	5·7
In controls ...	0·5	2·6	6·2	10·7	17·0	22·3	28·0	34·3

The Jensen's rat sarcoma used for these experiments was not growing with its usual vigour, but in spite of this the difference between the growth of the tumours in rats fed on vitamin-B complex and in the controls was maintained.

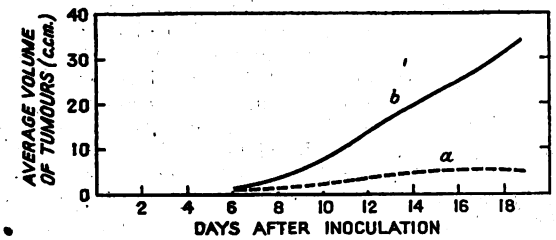

Fig. 3—Growth of tumours in (*a*) 18 rats (the offspring of parents on a normal diet) fed on dry yeast, bran, and marmite since birth compared with that in controls (*b*).

Group IV

For these experiments 103 young rats, whose parents had been fed on vitamin-B complex as in group I, were used, the only difference being that, when these rats were having special feeding, the supply of Glaxo yeast extract was not available, so dry yeast, bran, and marmite were given instead. The average volume of the tumours in the rats fed on vitamin-B complex, twenty days after inoculation, was just over a quarter of that in the controls (fig. 4):

	Days after inoculation						
	8	10	12	14	16	18	20
Average volume (c.cm.) of tumours:							
In 103 rats (offspring of parents fed on vitamin B) fed on dried yeast, bran, marmite, and aneurine.. ..	2·0	3·8	6·5	11·3	14·0	16·0	17·8
In controls	2·0	6·0	12·5	22·0	32·6	44·5	63·0

Group V

A few experiments were done on the same lines with a different type of sarcoma, one which occurred spontaneously in the femur of a rat which had been exposed to gamma radiation in its youth. Though the tumour originated in the bone just under the periosteum it has been very easily propagated in the subcutaneous tissues of rats for many years—in fact, it grows progressively in over 90% of cases. It is a slower starter than Jensen's rat sarcoma, and as a rule the rats do not have to be killed until six or seven weeks after inoculation. When using this tumour instead of Jensen's rat sarcoma it is more difficult to inoculate

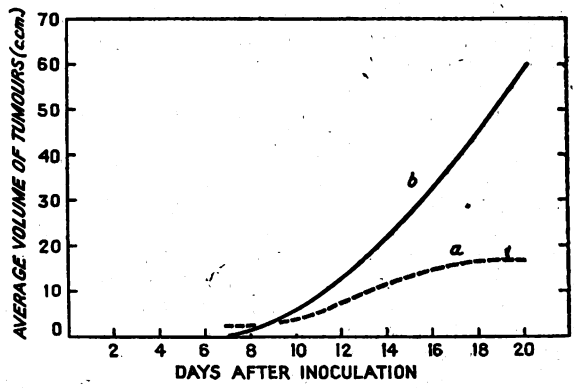

Fig. 4—Growth of tumours in (*a*) 130 rats (the offspring of rats fed on vitamin-B complex) fed on dry yeast, bran, and marmite compared with that in controls (*b*).

pieces of the same size and quality at will, as it is very soft and hæmorrhagic and breaks easily; and an accurate estimation of the size of the growth is most difficult, as nodules attached to the main tumour often appear.

A series of 59 normal young stock rats which had been fed on extra vitamin-B complex (yeast, bran, marmite, and aneurine) for eight weeks before inoculation were inoculated in small groups at the same time as the same number of controls, and the subsequent growth of the tumours was carefully measured. On the last day before any rats had to be killed owing to the size of the tumour, the average volume of the tumours in the rats fed on vitamin-B complex was less than half of that in the controls—39 c.cm. in the rats fed on vitamin-B complex against 87·5 c.cm. in the controls.

DISCUSSION

The results recorded here show that a rat's resistance to tumour growth may be increased by feeding it for some time on vitamin-B complex before inoculation of the tumour graft.

The first measurements of the tumour grafts were just as large in the rats fed on vitamin-B complex as in the controls; in fact the average volume of all the tumours in the 206 rats on vitamin-B complex at the first measurement was 0·83 c.cm. against 0·75 c.cm. in the controls.

The early stages of growth of Jensen's rat sarcoma were usually as rapid as normal in the rats fed on vitamin-B complex, but after ten days or a fortnight the rate of growth changed, ending in many cases with the eventual disappearance of the tumour.

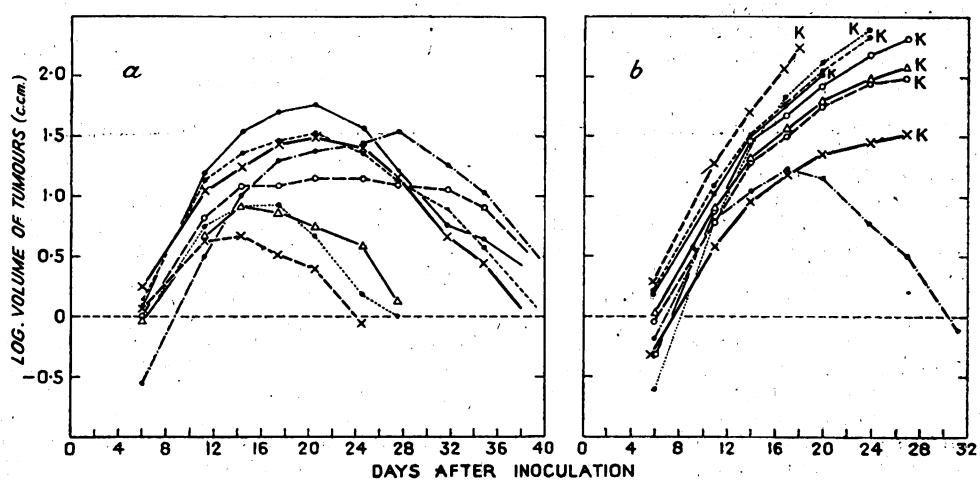

Fig. 5—Log. volume of tumours in (*a*) 8 rats (the offspring of parents fed on vitamin-B complex) fed all their lives on dried yeast, bran, and aneurine compared with that in controls (*b*); K, killed.

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A graph (fig. 5) showing the logarithmic rate of growth of Jensen's rat sarcoma in two families (8 rats), the offspring of parents fed on vitamin B and themselves fed on a similar diet, is typical of the usual sequence of events. It shows the normal rapid start of the tumour in the rats fed on vitamin B, followed by the sudden slowing down in the rate of growth and frequent disappearance of the tumour, in contrast to the more or less steady growth in most of the controls.

The tumours whose growth is depicted in fig. 5 were some of those included in fig. 4. The rats fed on vitamin-B complex were just three months old when inoculated, and the controls were of practically identical weights. After 18–20 days' growth, many of the rats bearing the larger tumours had to be killed; so the graphs of the average volumes cannot be taken to the final stages.

The greatest resistance to tumour growth was shown by the rats in group I, in which the average volume of the tumours in the rats fed on vitamin-B complex was only 0·17 of that of the controls 22 days after inoculation. The subsequent records show that 26 of the 31 tumours growing in the rats fed on vitamin-B complex disappeared.

The 103 rats fed on vitamin-B complex in group IV did not show quite so much resistance to the tumour as did those in group I, though they too were the offspring of parents fed on vitamin-B complex and had vitamin-B complex themselves all their lives. The average volume of their tumours was 0·28 of that in their controls, against 0·17 in group I. This slight falling off in the effect may be due to the fact that these rats were fed on dried yeast, bran, and marmite, which could not be standardised in the same way as the potent Glaxo yeast extract given to group I, and they probably consumed less vitamin-B complex than did those in group I.

As the feeding of the rats in group II on extra vitamin-B complex was begun only a few weeks before inoculation of the tumour, it is not surprising that the resistance shown by these rats was not so great as that of the rats fed on vitamin-B complex in group I, which had extra vitamin-B complex all their lives and were born of parents fed on vitamin-B complex.

In group III the Jensen's rat sarcoma was not growing with its usual vigour; the difference between the rate of growth of the tumours in the rats fed on vitamin-B complex and that in the controls was, however, maintained. The possibility of producing this resistance by merely feeding with extra vitamin-B complex after the tumour has become established has not yet been tested. Some families of rats have shown rather more resistance than others receiving the same diet, but on the whole the results have been very consistent. In America a high content of riboflavine in the liver of animals has been found to reduce the chance of tumour development.[3]

SUMMARY

The addition of vitamin-B complex to rats' normal diet of hospital scraps increased their resistance to the growth of Jensen's rat sarcoma.

In many cases the tumours in the rats on vitamin-B complex eventually disappeared, and the average volume about three weeks after inoculation was often less than a quarter of the volume of the tumours in controls.

A similar effect was obtained with a sarcoma of bone origin.

This resistance was also set up by three weeks' feeding on vitamin-B complex before the inoculation of tumour grafts.

Rats on the normal diet of hospital scraps with no additional vitamin-B have always appeared well-nourished and free from disease and have shown no obvious signs of deficiency of vitamin-B complex.

3. *Ann. N.Y. Acad. Sci.* 1948, 49, 1, reviewed in *Nature, Lond.* 1948, 161, 106.

RAPID DETERMINATION OF URINARY PREGNANEDIOL

A COMPARISON OF TWO METHODS

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IN view of the increasing interest in the possible clinical application of the results of urinary pregnanediol assays, and since for clinical use rapidity and comparative ease of performance are important desiderata, attention has been paid to the development of methods avoiding the tedium and man-hour consumption of the earlier techniques. Undoubtedly accuracy has had to be sacrificed for rapidity, but from the clinician's standpoint meticulous accuracy is not necessarily the prime requirement; if approximate results can be shown to have diagnostic or prognostic significance they will have laid a claim to recognition as being of clinical value.

The first of the rapid methods, that devised by Guterman (1944) and intended to be only semi-quantitative, has produced conflicting reports about its value as a diagnostic test for pregnancy (Guterman 1945, Morrow and Benua 1946, McCormack 1946, Reinhart and Barnes 1946, Mack and Parks 1947, Merivale 1948, &c.) but considerable agreement in so far as its prognostic value in threatened abortion is concerned (Guterman 1946, Bender 1947, 1948, Merivale 1948). That it is inaccurate there can be no doubt whatever, especially when small amounts only of pregnanediol are present, loss of material resulting from the rapid precipitation at low temperature as well as from the method of purification involving the use of 2% sodium hydroxide in methyl alcohol. Moreover, because a single precipitation is used, chromogenic material is liable to contaminate the precipitated pregnanediol. In an endeavour to reduce the inaccuracy, two modifications were introduced (Swyer 1947–48): (1) the precipitation was done during slow cooling, as advocated by Sommerville et al. (1947–48a and b), in a 37°C incubator over a period of two hours; and (2) the precipitation was repeated in precisely similar circumstances. These modifications considerably decreased the rapidity of the method and cannot be claimed materially to have increased its accuracy except perhaps in the prevention of spurious high readings.

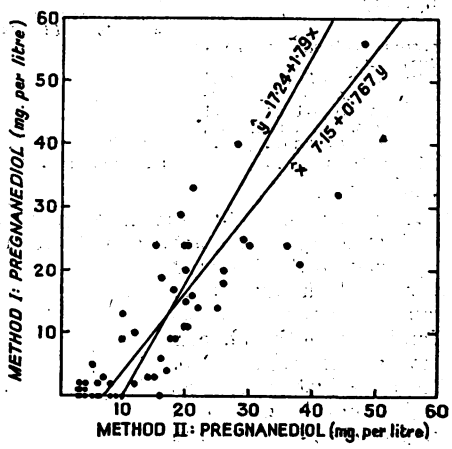

Fig. 1—The relation between the results obtained in 52 parallel pregnanediol assays by the modified Guterman technique (method I) and that of Sommerville, Marrian, and Kellar (method II).

A new rapid method has been introduced by Sommerville et al. (1948); this avoids the unsatisfactory purification procedure mentioned above, and is said to give relatively good recoveries even with small amounts of pregnanediol (though not with amounts of the order usually found in the luteal phase of non-pregnant women). Because this new technique seemed to be a notable advance from the point of view of its possible

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clinical value, it was considered to be worth while to compare the results obtained by this method with the modified Guterman procedure already mentioned. The results of this comparison, reported below, seem to be heavily in favour of the method of Sommerville and his colleagues.

EXPERIMENTAL

In the modified Guterman procedure (method I) the technique followed is precisely that described by Guterman (1944), except that precipitation from boiling *N*/10 sodium hydroxide is allowed to take place for 2 hours in a 37°C incubator. The precipitate is next filtered and washed as in the original method but is now dissolved in 10 ml. of hot acetone and then reprecipitated as before. Most of the acetone is allowed to boil off (two or three minutes on the hot plate) before transference to the incubator. Final solution in absolute alcohol, evaporation of the latter, and colour development with sulphuric acid follows the original technique.

Fig. 2—The relation between the results of method I and the difference between method II and method I.

The method of Sommerville et al. (method II) was followed according to their instructions. The coloured solutions were read with a Gambrell photo-electric colorimeter.

Fifty-two random urine samples have been assayed in parallel by the two methods, and the results are shown graphically in fig. 1. The correlation coefficient is 0·95 ($P>0·01$); hence there is a highly significant correlation between the results obtained by the two methods. Since neither variate can be determined without error, two regression lines (X on Y and Y on X) can be calculated, but these are not widely divergent, because of the high correlation coefficient. The equations are $\hat{Y} = -17·24 + 1·79X$, and $\hat{X} = 7·15 + 0·767Y$; it will be seen that they cut the X axis at $X = 7·15$ and 9·63 respectively; the mean value given by method II is therefore 8·4 mg. per litre when that of method I is zero. This suggests strongly that method II detects quantities of pregnanediol too small to be assayed by method I.

In an attempt to analyse further the relationship between the two methods, the results of method I have been plotted against the difference between methods I and II (fig. 2). The correlation coefficient is 0·48 ($P>0·01$) and, though less than that in fig. 1, is still highly significant. In spite of the rather wide divergence of the two regression lines ($\hat{Y} = 15·66 - 0·87X$ and $\hat{X} = 7·39 - 0·25Y$), it is clear that the difference between the two methods is greatest at high and low pregnanediol levels, being least at about 20 mg. per litre; below this level method II gives the higher reading, and above it method I.

To study the reproducibility of the results obtained by the two methods, four replication experiments were made. In each of these six 100 ml. aliquots of the urine sample were assayed, three by method I and three by method II. The results are shown graphically in fig. 3, from which it can clearly be seen that at lower pregnanediol levels method II gives far more reproducible results, whereas at higher levels the mean values of the two methods tend to approximate and the ranges to become similar. As a measure of the variability of the two

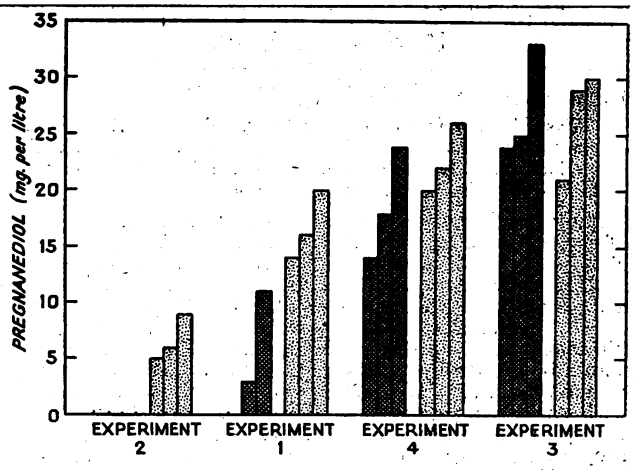

Fig. 3—The results of 4 replication experiments in each of which 3 urinary pregnanediol assays were carried out by each method: hatched columns, method I; stippled columns, method II.

methods in this experiment, the variances for all the readings by each method were calculated and found to be 145·51 and 75·9 for methods I and II respectively. By all criteria, therefore, method I gives less reproducible results than does method II.

DISCUSSION

The implication of these results is clear. The rapid method of pregnanediol assay devised by Sommerville et al. (1948) can detect quantities of pregnanediol too small for assay by the Guterman procedure and gives far greater reproducibility at low levels. At higher levels (over 20 mg. per litre) there is little to choose between the methods; but, since the clinician is more likely to be interested in cases where the level of urinary pregnanediol excretion is low, there seems to be little doubt that for clinical use the new procedure is greatly to be preferred, especially since it is very little more time-consuming than the original Guterman method.

As to whether or no the new method could be used in the detection of luteal activity in the normal menstrual cycle, some doubt remains which could only be settled by actual trial. It seems unlikely, however, that such a use would be valid, since on the one hand Sommerville et al. found the mean recovery of pregnanediol by their new method to be only 56·3% when the amount added to 100 ml. was 0·2 mg., while on the other hand the mean blank value obtained by me from five male urine specimens was 0·2 mg. per 100 ml. (which is considerably higher than that found by Sommerville et al.). These findings suggest that the results obtained in non-pregnant women would be varyingly unreliable.

The actual clinical value of pregnanediol assays is still far from settled. The relatively simple and rapid technique of Sommerville et al. may prove to be of great help in its investigation.

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Reviews of Books

Handbooks of Roentgen Diagnosis

The Skull, Sinuses and Mastoids. BARTON R. YOUNG, M.D., professor of radiology, Temple University, Philadelphia. Chicago: Year Book Publishers. London: H. K. Lewis. 1948. Pp. 328. 36*s*.

Professor Young has avoided the pitfalls in the path of those producing a handbook as opposed to a textbook. Too many such books have emerged as abbreviated textbooks with inadequate illustrations, or as mere atlases with a far from sufficient text. In this book the concise, full, and clear text is related to numerous good illustrations. The few omissions are of subjects which would be more appropriately placed in a larger textbook. The bibliography is perhaps too exclusively concerned with American journals and largely ignores the work of European, and especially Scandinavian, workers. The projections suggested for the mastoids and nasal sinuses ignore the possible use of a skull-table, with which subsequent, accurately comparative, views can be obtained. Intracranial conditions are not dealt with, except in so far as they affect the bony structure of the skull. The subject is not easy to treat concisely, but Professor Young has given full measure yet kept a proper balance.

Advances in Food Research

Vol. I. Editors: E. M. MRAK, University of California; GEORGE F. STEWART, Iowa State College. New York: Academic Press. 1948. Pp. 459. $7.50.

THIS is the first volume of a series which will provide authoritative reviews of every phase of food research by contributors of a high level of scientific competence. The major objectives of food research covered are the nutritional requirements of man, the physiological and psychological factors influencing food intake, the incidence of infectious and toxigenic agents in foods, and the effects of the processes through which foods are passed from harvesting or slaughtering till they appear on the table. In this volume are included contributions on the ageing of beef, vitamins in canned foods, voluntary food intake, the shelf life of dried eggs, palatability of poultry meat, deterioration of processed potatoes, climate and fertilisers affecting vitamin and mineral content of vegetables, browning of fruit products, food preservatives, and pectins. There is no doubt of the quality of the book, and successive volumes will be eagerly awaited. Of course the various reviews must be examined critically; in each article the facts are viewed through a personality, and the personality colours the landscape. For example, Lepkovsky, writing on voluntary food intake, draws inferences from the work of Orr and Gilks on the nutrition of two East African tribes, and from the work of Davis on the food choices of weanlings, exactly the opposite of those which other experts might draw. However, every cautious scientific reader keeps a wary eye on evidence, and it is for him that such works are published.

Sex Variants

G. W. HENRY, M.D. New York: Hoeber. London: Hamish Hamilton Medical Books. 1948. Pp. 1128. 40*s*.

THIS is primarily a collection of case-histories of male and female homosexuals in the United States. Many of these make instructive reading, but the conception and scientific direction of the research are less satisfactory. There is no indication of the method by which histories were selected; the extensive anthropometric and gynæcological data are not balanced by adequate psychometric tests; and it is difficult to see the object of the repeated seminal tests on male subjects. The histories appear in the patient's own words, and throw considerable light on the rôle of family background and lack of sexual instruction in producing variant behaviour; but many show signs of having been elicited by questions not mentioned in the text, and it is hard to estimate how far modification of detail has been permitted to preserve the confidence of the record. The interlocking of several histories makes it very difficult to assess them without further details of the group from which they are derived, and the classification into "bisexual," "homosexual," and "narcissistic" is open to criticism. There is no index or bibliography. The only conclusions are presented as a series of dogmatic aphorisms in the Hippocratic manner, though a further volume of conclusions is in preparation. The general result, while informative up to a point, is disappointing in view of the large amount of work the survey must have involved. English medical readers will find the book interesting rather as a series of psycho-analytical cases for diagnosis than as a picture of the mechanisms involved in sexual variation. The spirited attack in the preface on "justice tempered with ignorance and prejudice" will command wide support.

Studies in Analytical Psychology

GERHARD ADLER, PH.D. London: Routledge & Kegan Paul. 1948. Pp. 214. 21*s*.

BY means of half a dozen discrete papers Dr. Adler manages to give the impression that the reader has been taken on a conducted tour through the main passages of Jungian analysis. This impression is illusory, for analysis is essentially an emotional experience, and Dr. Adler is here applying an unemotional technique—controversial discussion and the presentation of a reasoned theme. Nevertheless, for the interested layman, no less than for the psychiatrist, there are no really dull pages. Dr. Adler, while scrutinising his subject matter with great care, never fails to convey also his profound respect for that subject matter—the individual human being. He is rightly allied with the school of thought calling itself individual psychology.

Deep Massage and Manipulation Illustrated (3rd ed. London: Hamish Hamilton Medical Books. 1948. Pp. 278. 17*s*. 6*d*.).—Dr. James Cyriax provides the physiotherapist with a clear illustration, opposite a brief precise description, of each of the varieties of deep transverse friction or passive movements he may be called on to make. Even the practising orthopædic surgeon will find the book useful in reminding him that there are some indications for passive treatment. Occasionally the teaching is questionable: it is hard to believe in no less than four distinct varieties of tennis elbow requiring different treatment; and forced flexion of the lumbar spine may not seem wise to all. But the book does exactly what it sets out to do, and is beautifully produced.

Remington's Practice of Pharmacy (9th ed. Easton, Pa.: Mack Publishing Co. London: Interscience Publishers. 1948. Pp. 1511. 90*s*.).—This classical work, unmistakably American in outlook and perspective, retains its pre-eminent place in the pharmaceutical world. Mr. E. Fullerton Cook and Mr. Eric W. Martin, the editors, have had the collaboration of more than forty associates. Several new chapters have been added, and those on biological assay, vitamins, amino-acids, and sex hormones are specially noteworthy. On both sides of the Atlantic serious students and practitioners of pharmacy in its many branches have come to regard this treatise as indispensable; and there will be many physicians who will covet the book as a work of reference, and value the concise statements on pharmacology and therapeutics now included.

Twelve Years with Roosevelt (London: Putnam. 1948. Pp. 241. 12*s*. 6*d*.).—Stricken in his prime by poliomyelitis, Franklin D. Roosevelt might well have allowed his political life to come to an end: but he set himself resolutely on the road to recovery, and later took infinite trouble to help the treatment of other sufferers from the disease. In this book Vice-Admiral R. T. McIntire, formerly physician at the White House, describes his ceaseless and anxious watch over the President's health. No doctor, in such circumstances, could expect fuller coöperation than Mr. Roosevelt gave; but he was not an easy patient, and it was sometimes hard to keep his abounding mental buoyancy in line with his physical capacity. The book gives an account of his habits of life and his general outlook, and shows that he inspired a deep affection in those who had most to do with him. Admiral McIntire studiously avoided being drawn into the political currents by which he was surrounded, but he provides an interesting study of the way in which a great man, helped by his wife, overcame adversity.

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THE LANCET

LONDON: SATURDAY, JAN. 15, 1949

The Agene Puzzle

IN December, 1946, Sir EDWARD MELLANBY reported that hysteria in dogs could be produced by feeding them on flour treated with agene (nitrogen trichloride), the flour improver and bleacher in common use for the past twenty-five years in Britain, the U.S.A., and many other countries. Intensive investigations were at once begun by teams of workers here and in America to see whether flour so treated was harmful to other animal species, particularly man. It was soon found that somewhat similar symptoms could be produced in cats, rabbits, and ferrets, while American workers claimed that though monkeys did not develop hysteria they showed other abnormalities. In rats, guineapigs, and hens, on the other hand, there were no ill effects whatever. And despite exacting tests no definite evidence of harm has so far been observed in man, even when the flour has been treated with doses of agene considerably larger than in normal commercial practice. However, after a public hearing by the Food and Drug Administration in October, at which scientific, medical, and milling interests were represented, the U.S. Government has prohibited the use of agene after Aug. 1, 1949, and has immediately sanctioned the use of chlorine dioxide as an alternative flour improver. This decision, contained in the *Federal Register* for Nov. 27, 1948 (p. 6969), has been reached despite the admission in the citation that "although the experimental work on humans is limited, no adverse effect as a result of foods prepared from flours treated with nitrogen trichloride has been found." That being so, the Food and Drug Administration could not have banned agene under the Federal food laws, and the decision was presumably taken by the express wish of the trade interests.

Flour treated with chlorine dioxide does not produce hysteria in dogs or other animals; nor, so far as is known, does it have any harmful action on man. Nevertheless, chlorine dioxide is an even more powerful chemical reagent than nitrogen trichloride; and in food manufacture there has been far less experience with chlorine dioxide than with agene. We understand that our own milling industry has already developed plant for generating chlorine dioxide if the biological research now proceeding shows without doubt that the change from agene is desirable. Nearly eighteen months ago we expressed this view: "At first blush it might be suggested that the use of agene as an improver in milling technique should be stopped, and it is true that there are possible substitutes. But a fuller investigation tends to discount any precipitate action. . . . We think rather that the whole subject should remain in the field of investigation, with the double approach by medical research and by industry." Research is still in progress, and it is not yet clear on what evidence our American friends have decided to introduce a new improver whose potentialities appear uncertain. Admittedly experiments completely justifying their action may be announced tomorrow; but further research may support those who doubt the wisdom of their decision. Meanwhile, as reported in our Parliamentary columns on Dec. 25, a scientific committee including Sir EDWARD MELLANBY and Sir WILSON JAMESON is reviewing the situation on behalf of the Minister of Food.

In substituting chlorine dioxide for agene the Americans have recognised the need, under modern conditions, for flour improvers. The need is even greater in Britain, where much of the wheat milled is, perforce, not of the best bread-making quality, and where, as in the U.S.A. but not some other countries, the bulk of the bread is made not by hand but in machine bakeries. Clearly further research is called for in the quest for an improver which by its very nature would be above suspicion. Ascorbic acid could be used, but even if the necessary quantity could be made its cost would probably be prohibitive. An intensive inquiry with the aim of finding a satisfactory biological (as distinct from chemical) improver would be well worth while. Much of the research now being done on agene is directed towards the isolation of the product, formed by the interaction of the gas with protein, which is responsible for the toxic effect on dogs. The isolation of this product should help to explain the toxic substance's different action on dog and on man, and should also throw light on the mechanism of flour improvers in general.

Vasotropic Factors and Shock

ON Jan. 1, writing on the circulation of the blood in healthy tissues, we referred to the new concept elaborated by ZWEIFACH and CHAMBERS, and outlined their views on how the flow of blood is controlled. By 1945 these two workers and their colleagues had also studied the peripheral circulation in certain kinds of experimental and traumatic shock. There was, they found, an initial stage of compensatory over-activity (enhanced contraction of the smooth muscle of the metarterioles and precapillary sphincters) calculated to preserve a basic blood-supply to the tissues and at the same time to ensure an adequate venous return. This stage was followed, in those animals that showed deterioration, by one in which there was decompensatory under-activity of the same smooth muscle, resulting in a diversion of blood to the tissues and to its stagnation within them. The participation of humoral factors was already being suspected when the team of investigators was enlarged by the addition of EPHRAIM SHORR, who has since become its leader in the more clinical studies. Soon afterwards the names of S. BAEZ (vascular surgery), R. F. FURCHGOTT (biochemistry), and A. MAZUR (chemical isolation studies) appeared, and more recently MARY A. PAYNE (liver disease) has joined them. Corresponding with these increases in personnel, there has been considerable widening of the scope

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of the joint researches. The conclusion that has been reached is, briefly, that the peripheral circulation distal to the arterioles is largely controlled by two "vasotropic factors" which have been styled "vaso-excitor material" and "vaso-depressor material." The latter has very recently[1] been shown to be a protein substance, ferritin,[2] or its iron-free portion, apoferritin. The time is therefore opportune for some review of these various researches and their implications.

Isolated-tissue studies have shown that the vaso-excitor material (V.E.M.) is produced in the cortex of the kidney when that part of the organ is rendered anaerobic, and that it is inactivated by the same part (and perhaps also, to a lesser degree, by the liver) when the supply of oxygen is once again adequate. The vaso-depressor material (V.D.M.) is produced mostly by the liver, but also by skeletal muscle and by the spleen, under anaerobic conditions: it is inactivated, aerobically, by the liver alone, and long-continued lack of oxygen will irreversibly depress the capacity of the liver to inactivate it. In the compensatory phase of shock the relative reductions of the renal cortical and hepatic blood-flows are such that the renal cortex is deprived of oxygen while the liver still obtains it. So production of V.E.M., but not of V.D.M., takes place. In the decompensatory phase V.E.M. is still produced, but the renal cortical blood-flow is too scanty to carry it into the general circulation. Simultaneously, the further reduction in the oxygen supply to the liver results in the anoxic production of V.D.M. So in the first phase of shock V.E.M. predominates, and in the second phase V.D.M.

In circulation, V.E.M. increases the frequency and amplitude of the constrictor activity (vasomotion) of the metarterioles and precapillary sphincters, and very greatly enhances their reactivity to the topical application of adrenaline (as tested in the mesocæcum of the rat and omentum of the dog). Hence it compensates for a reduced circulating blood volume by confining the peripheral blood-flow to the thoroughfare channels and ensuring an adequate venous return. V.D.M., on the other hand, progressively depresses the reactivity of the metarteriolar musculature and precapillary sphincters, with diversion of blood to the true capillaries, venular stagnation, and inadequate venous return. With consequent progressive lack of oxygen in the blood supplied to the liver, the natural mechanism for the production of V.D.M. comes ever more into play, and the mechanism for its inactivation slows down. So the shock becomes irreversible, and death ensues. To the above short account, we need to add the findings that V.D.M. has an antidiuretic effect; that an intact adrenal cortex appears to be necessary for the proper functioning of the V.E.M. mechanism; and that V.E.M. differs from renin in being heat-stable and dialysable, as well as in its more physiological properties, and also differs from hypertensin and similar pressor agents, which produce *acute* changes in blood-pressure by their constrictor effects on the *larger arterioles*. Though SHORR and his colleagues do not seem to have done so, we may add that the initial reaction in various kinds of shock—and one which will produce the hypoxic or anoxic conditions necessary for the production of V.E.M.—may be nervously intermediated; as, for instance, TRUETA et al. at Oxford found in their tourniquet experiments.[3] If, in the treatment of established shock, one of our basic aims should therefore be to restore the supply of oxygen to the liver, and so enable that organ to inactivate its own V.D.M., fresh interest will be taken in oxygen therapy, for which a plea is made by Dr. OHLSSON in our correspondence columns this week.

The rôle of the hepatorenal vasotropic factors in experimental renal hypertension and in human essential hypertension is considered by SHORR,[4] but his account cannot readily be summarised here. Before concluding this survey, however, we must make some reference to the hypothesis, which he and his colleagues have been developing, "that the vaso-excitor and vaso-depressor principles are oppositely acting components of a homeostatic mechanism participating in the regulation of peripheral blood flow and blood pressure."[5 6 7] While the articles written by these authors deal mainly with the drastic disturbances of equilibrium produced by experimental shock, they suggest that "under more normal circumstances, circulatory homeostasis would undoubtedly be accomplished by more subtle alterations in the equilibrium between these vasotropic principles."

Uses of Hypnotism

HYPNOSIS is repeatedly rediscovered as a therapeutic method. It is unfortunate that the relief of symptoms of functional nervous disorder, when it occurs under hypnosis, is often so striking—and sometimes so transient—that dispassionate appraisal, even by doctors, has been rare. Progress in its use has been hampered by an excess of enthusiasm, of condemnation, and of theoretical speculation. A hundred years ago THOMAS WAKLEY announced in THE LANCET that "we cannot publish any paper on the subject of such an odious fraud as mesmerism," and had reasons which seemed good at the time. JAMES ESDAILE, the Perth surgeon who had carried out hundreds of major operations under hypnosis, was unable to publish his results in the recognised medical journals. Before him JAMES ELLIOTSON, once a physician at St. Thomas's Hospital and the first to use hypnotism in a teaching hospital to secure sleep and for the relief of pain, had been obliged to resign his chair of medicine at University College, London, because his colleagues felt his enthusiasm to have exceeded rational bounds—as indeed it had. The phenomena of hypnosis have often attracted the attention of those who preferred mystical and occult speculations to the discipline of the scientific approach; and even today medical men who investigate the subject for themselves are apt to be suspect. It is to be recalled, however, that the study of hypnosis in the hands of such leaders of thought

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as CHARCOT, JANET, BREUER, and FREUD was the direct precursor of psychopathology as we know it today, and that current methods of psychotherapy owe much to the earlier work of schools, such as those of LIEBAULT [1] and BERNHEIM,[2] where hypnosis was the principal method of treatment for the functional nervous disorders. When FREUD turned away from hypnosis to develop the method and theory of psycho-analysis, the technique went out of fashion, though the need for rapid superficial results in the 1914–18 war led to its revival on a fairly large scale in the hands of WILLIAM BROWN, TROTTER, MCDOUGALL, YELLOWLEES, YEALLAND, and many others.

Despite its extensive clinical use, no fully satisfactory explanation of the phenomena of hypnosis has yet been advanced, though the experimental work of CLARK HULL and his associates and the observations of PAVLOV have added much to our knowledge. The view that hypnosis was in many ways identical with sleep has been seriously challenged by the electro-encephalograph. A publication of the Menninger Foundation, reviewed in these columns on Jan. 1 (p. 23), gives a summary of the present position. During the war, too, the Kretschmer school turned their attention to basic research on this subject.[3]

It is a pity that the clinical study of the applications of hypnotism which began in this country under BRAID has made uneven progress. The discovery of inhalation anæsthesia, with its greater reliability and lessened drain on time and energy, put an end to its use in surgical practice. None the less the knowledge of sympathetic rapport with the patient which comes with experience of the technique of hypnosis might frequently lead to smoother induction if anæsthetists knew something of the method. In psychiatric practice hypnosis has a limited but established place in diagnostic exploration and in treatment. The economics of psycho-analysis call for the use, as suggested by RADO [4] and others, of any means which will shorten the total time taken by the treatment. At the moment, doctors often enter psychiatric practice with no more than a superficial knowledge of the technique and indications for hypnosis. Those who are unlikely to undertake a long psycho-analytic training would find a sound training in the use of hypnosis, persuasion, and similar psychotherapeutic methods of value in exploring unconscious motivations.

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Annotations

HOW TO WRITE A REPORT

WRITING is a development of the art of speaking, as Dr. C. Leonard Williams pointed out at a meeting of the section of epidemiology of the Royal Society of Medicine on Jan. 3; and the writer who bears this in mind has a good natural defence against the virus of jargon. Reports, Dr. Williams thinks, should be positive, not vague, and the writer should know what manner of man he is: is he able to address large groups, or is he fitted to teach small bodies of students, or is he at his best with an audience of one? The first type can write for the general public, the second is fit to write exact and scientific reports, and the third should practise writing his reports as though they were personal letters to a friend. Armed with self-knowledge and a big blue pencil, knowing and believing in his subject, any man, in Dr. Williams's opinion, can write a report worth reading. For the rest, avoid mixed metaphors, pick your type, see your proofs in galley, and place your illustrations as carefully on the page as though you were putting a picture on the wall. He would always put statistics at the end of a report, except for a few essential figures in a neat cage, or a graph; and the ordinary public, he finds, cannot stand more than two lines in a graph.

Prof. A. Bradford Hill passionately defended statistics. He knows the sort of man he is—the sort of whom it was written, "speak to them in glowing terms of Jacob's ladder, and they will ask the number of steps"—and he is not to be fobbed off with a picture. Graphs, in his view, can be used to supplement a table if they make things clearer, but figures are fundamental. Graphs show rate, not size, and look the same whether 300 patients are affected or 3; and a skilful manipulator of graphs can make the unwary believe anything. Besides, some people like reading tables; while those who don't can skip them. Nowadays we are all imbued, he said, with the spirit of sampling, despite the recent regrettable lapse of the public-opinion polls; but writers of reports do not always remember to say how a sample was taken, or to ensure that their conclusions are in accord with their figures. As a classical discrepancy, he quoted a statute of George III which required half the penalties paid under the Act to be given to the informer and half to the poor of the parish; but the only penalty it allowed was 14 years' transportation. Finally, he begged for precision; and indeed accuracy and precision were warmly approved by all.

Recipes for making a good report are numerous. Dr. A. L. Banks holds that first one must decide whether a report is necessary at all; and that once it is undertaken it should be comprehensive and kill the subject stone dead: there should be no supplementary reports as an afterthought. The introduction should show what it is about, the text should carry the relevant facts, and the conclusion should be clear. If action is needed the report should say so clearly. Dr. Robert Sutherland believed in defining one's purpose beforehand. Is the report to give information? To overcome prejudice? To influence behaviour? Whichever it is, the opening should have a direct and immediate interest for the reader; and here he had the support of Sir Weldon Dalrymple-Champneys, who believes in beginning with a provocative assertion and justifying it afterwards. Colonel C. L. Pasricha recalled the advice of one of his lecturers: begin with a long historical introduction and scrap it; write the body of the report putting down all your data, and scrap that too; write a discussion and keep it; write a summary of your discussion, sleep on it; and if you think it worth while, publish the summary. Dr. William Hartston offered three prescriptions. A report to a health committee should contain the facts and all the facts; a report to a senior officer should contain selected facts; and a verbal report to students should contain one fact repeated three times. Dr. W. A. R. Thomson appealed for the removal of abbreviations, or at all events for the return of full-stops between initials, and for a course in logic for all medical students. Dr. William Gunn's proposal, made in defiance of Prof. Bradford Hill, that in published articles all protocols and tables should be omitted and sent to readers only on request, was countered by Dr. R. E. O. Williams who pictured the exasperation of the man looking up the reference twenty years later.

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NEW SURGICAL AND GYNÆCOLOGICAL FILMS

A SERIES of four films on the control of cross-infection during surgical dressings is being prepared for Imperial Chemical Industries, under the supervision of Dr. Leonard Colebrook. The first is introductory, the second and third consider channels of infection of small and large wounds, and the fourth deals with common mistakes. Parts 2 and 3 are finished. Part 2 says that in dressing small wounds the risk of cross-infection by airborne organisms is negligible, and that direct contact—as from dressers or instruments—provides a major risk. Two recommended routines are shown for changing dressings by the no-touch technique, first for the single-handed nurse, and secondly in a specially built outpatient department, with one doctor, assisted by three nurses and a secretary, passing cases to three teams of four nurses each. Part 3 says that in dressing large wounds (particularly burns) airborne infection can be a greater factor than contact. The specially designed dressing-station shown is supplied with bacteria-free air under positive pressure. Into this the patient is wheeled in his bed, all ward over-bedding having been replaced by a clean sheet only. He is masked and his hair covered, and then he is wheeled into the dressing-theatre where a team of two nurses and a doctor, supplemented by a nurse in the sterilising-room next door, attend to his wound. After 5 minutes, when the air has been completely changed, the next patient is admitted. Cultures are taken from a slit-sampler and from every wound and treatment is determined to some extent by the bacteriologist's report. This technique has already resulted in a big reduction in cross-infection.

Both of these films, made at the Birmingham Accident Hospital, are concerned more with broad principles of organisation than with details of local technique. In this they are greatly aided by the free use of models of the building and of puppets. They leave an impression of routines carefully planned and well executed, and the routines seem sensible and easy to carry out, provided you have the staff, equipment, and building; but there's the rub. Those who have had practical experience of cross-infection problems will note with sympathy or malicious satisfaction, according to taste, that even these experts have not prevented a nurse turning on a tap to clean her hands and then reinfecting herself when turning it off; and in another sequence a "contaminated" nurse clearly turns on an elbow-tap with her hand. It is not enough to plan for trained and intelligent staff; one must also so arrange matters that the tired or thoughtless cannot stultify the precautions taken by their alert and careful colleagues. Here primary planning of layout might benefit from the advice of the industrial psychologist and the time-and-motion study expert. On the point of detail mentioned the Board of Trade could help by making foot-taps more easily obtainable. Photographically the two films are good, though the consistently flat frontal lighting and the absence of close-ups are fatiguing to the observer; the commentary is clear and helpful. Part 2 runs for 15 minutes, part 3 for 28. Both are 16 mm., colour, sound, made by I.C.I., Buckingham Gate, London, S.W.1.

Two new films on gynæcological technique—*An Operation for Procidentia* and *Subtotal Hysterectomy*—have been produced by Mr. Stanley Schofield, F.R.P.S., in the department of gynæcology of the Middlesex Hospital. Both run for about 15 minutes. The photography is excellent; the producer has so trained his actors that they are never in evidence, and as a result a good view of the operation is obtained by the audience. There is an impression of haste, but perhaps this is due to speeding up in display. Colour effects are good, though the clear-cut image is absent, as always in colour films. Shots are taken at appropriate intervals from the time the patient is wheeled into the theatre until she leaves for the ward. The arrangement of the patient on the table is shown in detail (a notable omission in the hysterectomy film is the very necessary emptying of the bladder as a preliminary) and a still is taken of the arrangement of the instruments on their table. The operative technique is based on that described in Berkeley and Bonney's *Textbook of Gynæcological Surgery*. The experienced surgeon may learn much from such films, for he knows what to expect and is in a position to be critical. But the medical student would benefit by frequent stops enabling the lecturer to demonstrate or to emphasise particular points. Compared with attendance in the operating-theatre, a film has the advantage that everyone can clearly see all the steps of the operation, which can be fully explained. On the other hand it can never give the student the full benefit obtainable from actually assisting at an operation on a patient whose history he has taken, whom he has already examined, and whose recovery he is going to observe.

DIETARY TREATMENT OF HEPATIC CIRRHOSIS

EXPERIMENTAL work has proved beyond doubt that nutritional deficiency may lead to a diffuse fibrosis of the liver indistinguishable from Laennec's cirrhosis.[1] This condition is almost always preceded by severe fatty infiltration, the extent of which is closely correlated with the rate at which the cirrhosis develops.[2] The nutritional factors that are most important in preventing an undue accumulation of fat in the liver are choline and methionine, either of which, in animals, will prevent both the infiltration and the consequent cirrhosis.

Attempts to treat cirrhosis of the liver on the lines indicated by these experimental results have been made chiefly in the United States. The diets used have been rich in protein and of high caloric value, and have contained additional vitamins and sometimes also additional choline and methionine. Patek,[3] who introduced this form of therapy, has described 124 cases of cirrhosis treated and observed during a 10-year period, and has compared them with a control group of 386 cases seen between 1920 and 1940. In the treated group the duration of life was significantly greater. Thus at the end of 1, 2, and 5 years the survivors in this group totalled 65%, 50%, and 30% of the original number of patients, whereas the corresponding figures for the control group were 39%, 21%, and 7%. Not every report is as favourable as Patek's, but most record significant improvement with this therapy, especially in cases with short histories and large livers. The better prognosis with large livers is readily understandable if the success of the diet really derives from the action of its lipotropic factors in removing fat from the liver; for the shrunken, atrophic liver, which is almost always poor in fat, cannot be expected to respond to these agents. This would also explain the poverty of response in cases of long standing, where fat tends to disappear from the liver.

Most of the experimental work on cirrhosis has been concerned with the production of the disease: comparatively little attention has been paid to factors affecting recovery. Yet as long ago as 1936 Cameron and Karunaratne[4] recognised that in rats cirrhosis induced by chronic carbon tetrachloride poisoning may

1. Blumberg, H., Grady, H. G. *Arch. Path.* 1942, **34**, 1035. Leading article, *Lancet*, 1948, ii, 221. Chalkoff, I. L., Elhorn, K. B., Connor, C. L., Entenman, C. *Amer. J. Path.* 1943, **19**, 9.
2. Glynn, L. E., Himsworth, H. P., Lindan, O. *Brit. J. exp. Path.* 1948, **29**, 1.
3. Patek, A. J., Post, J., Ratnoff, O. D., Mankin, H., Hillman, R. W. *J. Amer. med. Ass.* 1948, **138**, 543.
4. Cameron, G. R., Karunaratne, W. A. E. *J. Path. Bact.* 1936, **42**, 1.

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disappear spontaneously after withdrawal of the drug; and an investigation in Best's [5] laboratory has now shown that here again much depends upon the lipotropic factors. With diets deficient in these factors the condition deteriorated and the animals died within a few weeks; whereas with the addition to the diets of choline, methionine, or casein there was progressive improvement and virtual return of the liver to normal after a few months. Further supplementation of diets already adequately provided with lipotropic factors did not enhance the therapeutic effect—an observation that might be taken to indicate that in man the addition to the high-protein diet of choline or methionine is unnecessary. In many cases of cirrhosis, however, anorexia is prominent at the start of treatment, making it very difficult to achieve sufficient protein intake. Here supplements of choline and methionine might prove invaluable.

OVERTONES OF MUSIC

THE mind is only accessible through the senses, and it is well enough known that music can influence moods. So can sights and smells; and indeed smells are thought by many to be the strongest evocants of memory. Bearing in mind the sights, and occasional smells, of mental-hospital wards, even before the days of staff shortages, some will regard as a forlorn hope a recent attempt [6] to use music, alone of sensuous experiences, as a form of group therapy. Dr. Mitchell and Dr. Zanker, who made the attempt, recall that Pythagoras is said to have cured many mentally ill patients with music; and even to have devised melodies against despondency, anger, and desires. Their own experience, if less striking in its results, is uncommonly interesting. The group of about 14 patients of both sexes met as a rule in a small hospital library and included cases of neurosis, schizophrenia, paranoid states, and manic-depressive psychosis. They were mainly young or middle-aged. The sessions were held once weekly for an hour, which can hardly be regarded as massive dosage; though extra sessions were occasionally held when group members wished to hear a single long work again. A gramophone with pick-up was used, sometimes supplemented by the group with percussion or singing. Works were chosen to cater for all tastes and to represent all schools of composition; and after a few months a lecture-recital was given monthly, illustrating the history of musical development. Patients were asked whether they liked each work, and to give their reasons, as well as any special emotions or thoughts it provoked; and group discussion followed, not only on music but on personal and general problems. The observers found that some types of music favour "group cohesion" and "interpersonal, including doctor-patient, relationships"; and that sometimes music eased emotional release and made for "better integration of personality." These effects, they note, "represent a therapeutic gain, as a substitute for, and in addition to, individual psychotherapy." The patients, then, became easier and more friendly in response to certain kinds of music. They responded to the architectural and formal structure of the classical style by an increased feeling of security, equally well known, as the authors might have noted, to the sane. The romantic style brought emotional release, especially of inhibited sensuous experience; but many patients, especially of the inhibited types, felt unable to integrate the thoughts and feelings aroused—being presumably in that state of mingled excitement and yearning which again is familiar to the normal mind on hearing some compositions. Impressionistic music stimulated interest in the more withdrawn patients but had no special therapeutic value. Serious contemporary music, by such composers as Stravinsky, Bartók, and Varèse, was sometimes powerful enough to bring repressed unconscious forces into the consciousness of inhibited schizophrenic patients. Integration of the mind was not necessarily fostered, however, and might even be hindered because the patient could not come to terms with the emotions aroused. Modern dance music had little effect, but the whole group responded with greater friendliness and ease to traditional music and folk songs. These, though they stir up archaic forces in the mind, are it seems strongly integrating. Attempts at personality reconstruction, the observers conclude, may be made by appealing to "the fundamental human need for shape": the need, in short, for form and beauty. Must this appeal be confined to what enters by the ear?

5. Sellers, E. A., Lucas, C. C., Best, C. H. *Brit. med. J.* 1948, i 1061.
6. Mitchell, S. D., Zanker, A. *J. ment. Sci.* 1948, 94, 737.

EPILEPSY IN CHILDREN

DURING the last few years a concerted attempt has been made in America to replace the widely held gloomy picture of epilepsy by something more cheerful, and two large lay societies sometimes seem to vie with each other in laying on the bright colours. Peterman,[1] in an article on epilepsy in childhood, holds that this optimism is in danger of being overdone and has already led to disillusionment and disappointment. Talks of "miracle treatments" and the "knockout blow" are premature, and the prognosis of spontaneous regression often given to parents of children with petit mal is unjustified, since many such children go on to major fits in later life. Epilepsy, says Peterman, is a chronic inherited disease, present before the child is born, and even if clinical manifestations never develop "the defective gene will be transmitted regardless." Therefore the only hope for eliminating epilepsy lies in eugenics, and a limitation of the progeny of epileptics—a rather surprising conclusion, for surely the whole 12% of the population who are dysrhythmics, and therefore potential transmitters, should come under the eugenic ban? Discussing causation, Peterman, using canine hysteria due to agenised flour as an analogy, makes the interesting suggestion that there may be food factors at work precipitating or activating convulsions in predisposed subjects.

He lays great stress on the value of the E.E.G., which should be recorded in every case. In petit mal, for instance, the type of record will indicate whether only petit-mal medication is needed, or whether underlying activity of the grand-mal type is present as well, indicating a modified prognosis and the addition of a different drug. He uses the E.E.G. as the criterion for evaluating therapy and thus for determining the time when it is safe to stop treatment, and also for sorting out the cases of syncope and behaviour disorder which are epileptic in nature and will respond to anti-epileptic treatment. He accepts the findings of Gibbs and Fuster [2] that E.E.G.s should be recorded during sleep, whenever possible, because sleep records are much more reliable and informative. In treatment Peterman is still a firm believer in the ketogenic diet, which he regards as easily the most effective agent we have for the control of any and every type of epileptic fit. He claims that in 50% of epileptic children the attacks can be stopped by dietetic treatment. This is an unfashionable view, for there is a good deal of evidence that the ketogenic diet is falling into disuse. In this country a special permit would have to be sought to obtain the necessary fats, and there is some doubt if it would be granted. Peterman, however, speaks from long experience, and recent support for his views comes from Holland, where Kloek and Ledeboer [3] find the diet more effective than tridione in petit mal. At the Mayo Clinic Keith [4] records the best

1. Peterman, M. G. *J. Amer. med. Ass.* 1948, 138, 1012.
2. Gibbs, E. L., Fuster, B. (to be published).
3. Kloek, J., Ledeboer, B. C. *Ned. Tijdschr. Geneesk.* 1948, 92, 485.
4. Keith, H. M. *Amer. J. Dis. Child.* 1947, 74, 140.

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results in the treatment of major and minor epilepsy in childhood with the ketogenic diet, which he shows to be twice as effective as phenytoin or phenobarbitone, either singly or in combination. Drugs should only be used, in Peterman's view, if the ketogenic diet is impractical or impossible. Petit mal may then be treated with 'Tridione'; with 'Paradione,' a close relation of tridione that may also cause trouble in the bone-marrow occasionally; or with 'Thyphenytoin,' one of the hydantoins, which is useful in both grand and petit mal and less toxic than phenytoin. When tridione or paradione are used, phenobarbitone should be added to prevent the occurrence of major fits. For the latter, Peterman believes phenobarbitone to be the most reliable and effective drug, with the lowest incidence of side-effects. Thus it is doubly superior to phenytoin, the efficacy of which he holds to have been greatly exaggerated.

PENICILLIN AUGMENTATION IN BACTERIAL ENDOCARDITIS

BACTERIA vary considerably in their sensitivity to penicillin, from those, such as the hæmolytic streptococcus, which readily succumb, through a number of less sensitive organisms to the coli-typhoid group and others, which are scarcely sensitive to this antibiotic at all. Before the introduction of penicillin, subacute bacterial endocarditis was one of the almost invariably fatal diseases, though a small proportion of successes with sulphonamides had broken its spell. As soon as enough penicillin was obtainable it was used in an increasing number of cases. The dosage required was very high, relapses commonly necessitated a further course, and by then the causative organism had often become less sensitive to the drug. *Strep. viridans*, the usual causative organism, belongs to the intermediate group of bacteria which are rather less sensitive to penicillin, and heavy dosage is also necessary to enable an effective concentration of penicillin to penetrate the endocardial vegetations. In this issue Professor Stuart-Harris and his colleagues report on the effect of combining penicillin with 'Caronamide' to obtain a higher blood-level of penicillin. Two patients remained well for 5 months after this combined therapy when they had relapsed after repeated courses of penicillin alone; while in a third case a brief course of caronamide during penicillin therapy led to clinical improvement which had not occurred before.

Caronamide (4'carboxyphenylmethane-sulphonanilide) blocks the excretion of penicillin without noticeably damaging the kidneys.[1] Toxic symptoms recorded during caronamide therapy are transitory renal disturbances, with albumin and occasional red cells in the urine, while a few cases have developed rashes. In the present cases all there patients complained of nausea, which was eased by phenobarbitone. The dosage adopted was 4 g. four-hourly; perhaps if the caronamide had been given at the same rate of 1 g. per hour but more frequently than four-hourly this symptom might have been less troublesome. One patient had fever and leucopenia but no rash, and lumbar œdema was noted in 2 cases. This suggested some temporary renal impairment, but the urea-clearance test at the time was normal and the œdema soon subsided. In resistant cases anatomical peculiarities may hinder the diffusion of the penicillin into the endocardial vegetations; this may explain the failure in the first case. Caronamide is precipitated in an acid urine (below pH 5·5), so it may be desirable to alkalinise the urine, and a daily urinary output of at least 1500 ml. should be maintained while the caronamide is being given.

1. Beyer, K. H., Russo, H. F., Patch, E. A., Tillson, E. K., Shanes, G. *J. Pharmacol.* 1947, 91, 272. See leading article, *Lancet*, 1948, i, 70.

UREA-SULPHONAMIDE THERAPY

IT was in the 1914–18 war that urea was first used for the treatment of infected war wounds. Then it seems to have fallen into disuse until 1937, when Holder and Mackay [1] reported the effective treatment of infected or potentially infected wounds with sulphonamide-urea mixtures containing about 10% of urea. These workers claimed that urea was non-irritating to tissues and exerted its beneficial action by dissolving the pus and necrotic debris of wounds, which contains sulphonamide inhibitors. They also showed that urea increases the solubility of sulphanilamide and sulphadiazine in tissue fluids and that in vitro the bacteriostatic effect of sulphanilamide against *Bact. coli* is increased tenfold by the addition of 5% urea. Tsuchiya and his co-workers [2] extended these observations to other sulphonamides and showed in vitro that urea significantly increases their bacteriostatic effect even in the presence of known sulphonamide inhibitors such as *p*-aminobenzoic acid and methionine. Perhaps more important, they demonstrated that strains of sulphathiazole-resistant staphylococci in a synthetic medium were susceptible to combinations of urea and sodium sulphathiazole.

The development of sulphonamide resistance has now become of considerable practical importance in therapeutics, and any agent which may overcome this resistance deserves careful study. The local use of urea with sulphonamides is now well established, but urea is likely to be of greater therapeutic value in the treatment of sulphonamide-resistant infections, particularly those not amenable to treatment with penicillin. Apart from increasing the bacteriostatic action of the sulphonamides, urea increases their solubility, so that large doses can be given without fear of crystalluria. La Londe and Gardner [3] have treated five cases of meningitis with urea and sulphadiazine. The adult dose of urea was 30 g. four-hourly by mouth. One case was due to *Bact. fæcalis alkaligenes*, which did not respond to penicillin and sulphadiazine alone, and in which streptomycin was not tolerated. Another was a case of meningitis due to *Friedländer's bacillus*, which developed while the patient was receiving prophylactic doses of penicillin. There were also two cases of meningitis due to *Bact. coli* and one probably due to *Staphylococcus albus*. There was good evidence that the urea-sulphonamide therapy was responsible for these patient's recovery, and since it is simple, safe, and inexpensive it merits trial in sulphonamide-resistant infections before resorting to streptomycin.

MILEAGE FUND INCREASED

URGENT representations on behalf of rural pracititoners were made by the general medical services committee of the British Medical Association at a meeting with the Ministry of Health on Dec. 22. The Ministry has responded by raising the Mileage Fund, now standing at £1,300,000 per annum, to £2,000,000, the increase being retrospective from July 5. Of the £700,000 increase, £200,000 comes from the Special Inducement Fund and £500,000 is new money. The change means that the total sum now paid to rural practitioners for mileage will be about four times as large as that paid under National Health Insurance. If as many as a quarter of practitioners were defined as rural, the average sum drawn by each would still be nearly £400. At the cost of removing half of the Special Inducement Fund, the new arrangement will bring help to many of the doctors with relatively small practices who have been hit most hard by the loss of private patients. But not to all.

1. Holder, H. G., Mackay, E. M. *J. Amer. med. Ass.* 1937, 108, 1167; *Milit. Surg.* 1942, 90, 509; *Surgery*, 1943, 13, 677. See also Muldavin, L. F., Holtzmann, J. M. *Lancet*, 1938, 1, 549.
2. Tsuchiya, H. M., Tenenberg, D. J., Clark, W. G., Strakosch, E. A. *Proc. Soc. exp. Biol., N.Y.* 1942, 50, 262; *Ibid*, 51, 245.
3. La Londe, A. A., Gardner, W. J. *J. Amer. med. Ass.* 1948, 138, 406.

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Special Articles

MEDICAL TECHNOLOGY IN BRITAIN AND AMERICA

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MEDICAL technology may be defined as the work done by technicians in the laboratories of hospitals and medical schools. Its scope is as wide as that of the medical sciences themselves; and, though most technicians work in some branch of clinical pathology, a considerable number are engaged in work unconnected with disease—for example, in laboratories of anatomy and physiology. Technicians relieve the medical scientist of much work in both hospital and university, and they constitute in fact an auxiliary profession comparable with nursing. Medical technology has not achieved the same degree of general recognition as nursing, for several reasons. Medical technology is of necessity less in the public eye, and its nature and importance are consequently less widely understood than nursing; as a profession it is also much younger, and its educational plans are not yet fully realised.

The recent grant of public funds for training in medical technology is an important milestone in the history of the profession and a suitable occasion for a review of current methods and problems in the training of medical technicians.

TECHNICAL TRAINING IN BRITAIN

Technical skill is acquired by experience supplemented by systematic instruction. The occupation is entered by school-leavers of both sexes, and their educational background varies considerably. Possession of a School Certificate is increasingly common and is coming to be regarded as a suitable minimal requirement. Junior technicians normally attend night schools for some years; chemistry, physics, and mathematics are the chief subjects of study, and some technicians eventually obtain the External B.Sc. Lond.

The professional body for technicians is the Institute of Medical Laboratory Technology, which in 1942 succeeded the Pathological and Bacteriological Laboratory Assistants' Association (founded in 1912). The Institute works in close coöperation with the Pathological Society of Great Britain and Ireland, and contact with pathologists is further maintained through a standing committee of the Institute, the Pathological Society, and the Association of Clinical Pathologists. The Institute, like the earlier Association, holds examinations in various branches of medical technology.

A candidate for ordinary membership must be 20 years of age, with three years' experience of technical work, and must pass an intermediate examination in the elements of medical technology. After 2 more years' experience the student may obtain the associateship by passing a final examination in any one of four branches of medical technology—(1) pathological technique, (2) bacteriological technique, (3) chemical pathology technique, or (4) hæmatology and blood-transfusion technique. The fellowship is normally obtained by passing the final in a second branch, but exceptionally it may be obtained by writing a thesis. The final examinations are written, practical, and oral, and are conducted in various local centres with the assistance of pathologists, bacteriologists, and chemical pathologists. Medical technology is not a closed profession, but possession of the Institute's qualifications is a considerable advantage, since salary scales have been related to them.

TECHNICAL TRAINING IN AMERICA

Technical training and certification in the United States have developed on the same general lines as in this country but show some of the distinctive features of the American educational system. About the time of the first world war the demand for technical services led to the founding of schools run for profit. The need for competent control of technical education led to the establishment of the Registry of Medical Technologists by the American Society of Clinical Pathologists in 1928, and the inspection of schools for technicians was later undertaken by the American Medical Association.

The Registry grants six certificates after examination—a general certificate (discussed below) and five special certificates. The special certificates and the requirements for them are as follows:

(1) *Medical Technologist "Junior Grade."*—High-school education, a year's training in a hospital laboratory, and a year's experience.

(2) *Limited Certificate in Tissue Technique.*—High-school education and a year's experience of histological technique.

(3) *Limited Certificate in Chemistry.*—Bachelor's degree in chemistry and a year's laboratory experience of chemistry.

(4) *Limited Certificate in Bacteriology.*—Bachelor's degree in bacteriology and a year's laboratory experience of bacteriology.

(5) *Specialist in Bacteriology.*—Master's degree in bacteriology and three years' bacteriological experience in a medical laboratory.

The *General* or *Medical Technologist Certificate* was for many years the only certificate granted. The preliminary educational requirements are either (*a*) 2 years' work at a college, including chemistry (general and quantitative) and biology or bacteriology, if possible with physics and organic chemistry; or (*b*) graduation from a school of nursing, with a year at a college (including chemistry and biology). These are only minimal requirements, and candidates often possess a college degree (discussed below). The candidate must take a full-time course of technical training for at least twelve months at a school approved by the American Medical Association. The subjects of study are biochemistry, hæmatology, bacteriology, parasitology, histology, serology, and record-keeping. A model curriculum published by the Registry includes a time-table for courses lasting 12, 18, and 24 months. The time-table recommended for a 12-month course is as follows: urinalysis, sputum, fæces, and gastric contents, 6 weeks; hæmatology, 7 weeks; bacteriology, serology, and parasitology, 17 weeks; chemistry, 13 weeks; histology, 6 weeks; basal metabolism, 2 weeks; records, 1 week.

The schools for technicians are approved medical schools, general hospitals, and state health laboratories associated with hospitals. The conditions on which schools for technicians are approved are numerous and detailed but amount to a common-sense requirement that the student shall be competently taught under satisfactory conditions.

COMPARISON OF BRITISH AND AMERICAN TRAINING

To compare the scientific education of fully qualified British and American technicians it is necessary to explain briefly the nature of an American college. This is an institution giving advanced general education and has no British equivalent. A college has features of both school and university and gives a 4-year course leading to the degree of Bachelor of Arts (A.B.) or Bachelor of Science (B.SC.). The standard of these degrees is probably about the same as the pass standard of their British namesakes, but the range of knowledge required for them is wider and less directly vocational. The prospective American technician studies for 2–4 years at a college, and when he leaves it his educational standard

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probably ranges from that of a British Higher School Certificate to that of a British pass degree. When he starts his technical course, therefore, the American normally has a better scientific background than the Englishman has when entering technical work. On the other hand, the British technician continues his study of science at a night school and in the end probably overtakes the American.

The chief difference between the two systems of training consists in the fact that the British technician studies scientific and technical subjects concurrently, whereas the American completes his scientific studies before starting his technical course.

In both Britain and America there is a close parallelism between the education of medical technicians and of medical students. In Britain, studies of any subject are by comparison leisurely and prolonged, and both pure and applied science are studied concurrently, whereas in America the various subjects are studied over a shorter period and more intensively, the study of pure science being virtually completed before that of applied science (technical or clinical, as the case may be) is taken up.

Another important difference is in the scope of the technical studies. The British technician, after studying the elements of medical technology, specialises in one branch for several years before presenting himself for examination in it, whereas the American covers the whole field in one year. The certificate given at the end of the American course seems to indicate rather a general acquaintance with the subject than the high standard of skill required of the candidates for a British certificate.

The American special certificates, with their widely varying requirements, reflect the need of very different types and grades of technical skill, and by their recognition of specialism represent a move in the direction of the British system of certification. In the long run the American special certificates may well prove more useful than the older general certificate.

It is noteworthy that holders of even a master's degree rank as technicians rather than as independent scientific workers; for recognition as such in America the indispensable qualification is the degree of Doctor of Philosophy.

GENERAL EDUCATION OF TECHNICIANS

Many capable technicians have had relatively little general education, and it would be difficult to maintain that technical proficiency depends on scholastic attainments. Medical technology is a craft in which the indispensable requirement is fine manual skill; whatever else he may be the technician must be a skilled artisan. Since general education has no obvious bearing on technical competence, it might be argued that the prescription of standards of general education for technicians is unreasonable and needlessly restrictive of the field of recruitment. This would certainly have to be admitted if technical proficiency were all that is required of a technician, but in fact much more is required. The modern technician has responsibilities and obligations that do not differ in nature from those of the doctor or nurse, and his general education ought therefore to be at least comparable with that of other professional men.

Accuracy, methodical work, and awareness that mistakes may have serious results for patients are all expected of the technician as a matter of course; and outside his strictly technical work the technician must learn how to keep records and accounts, to estimate and order the supplies needed by a laboratory, to conduct correspondence with business firms, to deal courteously and tactfully with callers of many kinds, and, if need be, to work outside his normal hours without complaint. These and no doubt many other duties call for a professional outlook based on a good general education.

The standard of general education now required of candidates for examination by the Institute of Medical Laboratory Technology is the equivalent of the General Schools Certificate of the University of London, though other evidence of general education may be considered. The developments in progress in the British school system and the method of certification of those leaving school may well necessitate a new definition of the standard. The present standard, like any other beyond that of the lowest school-leaving age, may lead to the exclusion of competent technicians from the Institute's examinations, since employers may not always be able to find young people with a School Certificate or its equivalent. Such technicians could of course work for a certificate of general education but only under conditions more difficult than those at school and in the face of growing scientific and technical interests. The growth of a group of competent technicians ineligible for the Institute's examinations seems inevitable under present conditions.

It is not desirable to prescribe subjects for special study in a course of general education, whose aim should be intellectual development and not preparation for any particular career. An interest in science at school may well play a part in determining the choice of medical technology as a career, but the study of science because of its bearing on medical technology can be deferred until the career has been entered on. If any subject is worthy of special attention at school it is English, for skill in speaking and writing is an obvious advantage in any profession.

DEVELOPMENTS IN TECHNICAL EDUCATION

Training Schemes

It is evident to examiners that technicians often have difficulty in preparing themselves for examination, and the proportion of failures is high. The difficulty is due not to incapacity on the part of the candidates but to limited opportunities of gaining experience and to lack of systematic instruction. In the matter of experience, technicians in universities or large hospitals are not necessarily more fortunately placed than those in smaller institutions, since it is not usual for them to work outside their own laboratories. Technicians as well as examiners are aware of these handicaps and do what they can to overcome them; they sometimes manage to work in other laboratories or to obtain tuition from pathologists or senior technicians. Such opportunities should not have to be sought as a favour but should be readily available to all technicians. This has been widely recognised for some years at least, but it has become increasingly clear that the administrative problems involved in meeting the need are beyond the powers of individuals.

The main problem has been recently solved by the recognition of medical technology as a subject of public instruction under the "further education" schemes administered by local education authorities for the Ministry of Education. Schemes of training are already in operation or in process of organisation. It should now be possible without difficulty to obtain the use of all suitable laboratories in a whole district for teaching and to ensure that the syllabuses are fully covered under skilled supervision. These new opportunities will no doubt be reflected in future pass-lists and should greatly enhance the attractiveness of medical technology as a career.

Research Facilities

The work of technicians in clinical pathology is subject to natural limitations which vary with the type of work. Bacteriological, chemical, and hæmatological examina-

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tions often yield numerical or other direct results that the technician can himself report; in morbid anatomy, on the other hand, the technician's work ends with the preparation of a section which can be reported on only by a medical man with special experience. The interpretation of results—the assessment of their bearing on diagnosis, prognosis, and treatment—is properly a task for the clinician, assisted, if necessary, by the clinical pathologist.

Despite such limitations, which apply chiefly to routine hospital work, a large field remains open to the technician; in particular, chemistry and bacteriology can both be pursued as independent sciences. Most technicians may not have the time or inclination for research, but they should be aware of the educational value of studying a scientific problem. The planning and execution of simple experiments under skilled supervision and the discussion of the results in the form of an essay or thesis are a most useful exercise. The exceptional man should find it possible to work for the M.SC., either after graduation as a B.SC. or under special regulations applicable to non-graduates.

Foreign Study

A further opportunity should be open to the technician of some experience—that of working in a foreign laboratory. The opportunity would be especially valuable for those who will be much concerned with teaching under the new training schemes, but no technician could fail to benefit from it. The technician who has worked in several laboratories in this country and broadened his knowledge by reading and attendance at meetings should be well qualified to compare British and foreign practice critically. There is much to see and to discuss with foreign colleagues—the design and equipment of their laboratories, the range of their work, their technical methods, and their professional problems. Though even a short visit, such as is made possible by a holiday, would be valuable, the wider knowledge and deeper insight that are desirable could be obtained only by residence abroad for about a year—not an excessive period considered in relation to the whole of a working life. There is a wide choice of suitable places to visit, in both Europe and America. No-one need be deterred from choosing a Continental laboratory because he is not a linguist, for the use of English is widespread abroad, not least among scientific workers. On the other hand, anyone wishing to learn a foreign language could desire no greater opportunity, and the technician who made good use of his time would return home richer not only in professional knowledge but also in sympathetic insight into the life, thought, and problems of a foreign people.

If technicians are to enjoy these opportunities, which are nowadays open to many other types of professional worker, scholarships must be provided to cover the cost of travel and maintenance. Many foreign countries now offer scholarships for British subjects, and some of these may possibly be open to technicians; if not, representations could no doubt be made in appropriate quarters. Though the award of scholarships to British subjects by foreign countries is most helpful and greatly appreciated, we should not have to depend wholly on them for the higher education of our own countrymen; the primary responsibility for providing the necessary funds clearly rests on the educational authorities of this country.

Additional Examinations

The desirability of instituting examinations in additional branches of medical technology is sometimes discussed. With the recent addition of the examination in hæmatology the needs of technicians in clinical pathology seem to be well provided for, and discussion centres mainly round the question of examinations for technicians in anatomy, physiology, and pharmacology.

At first sight there certainly seems to be a case for instituting such examinations, which would serve as a stimulus to junior technicians and strengthen their professional position among the employees of universities. Experience, however, has shown that there are difficulties in the way of such developments. First, the candidates for any special examination would probably be much fewer than for the existing examinations, and the difficulty of providing instruction for them would be correspondingly greater. Secondly, it has not so far proved possible to reach agreement on what should be required of the candidates. Physiology, in particular, comprises such a wide variety of techniques that no two laboratories would probably agree on a syllabus. In anatomy the field of technical work is probably narrower, though the wide interests of modern anatomists have reduced the difference.

The work of technicians in anatomy, physiology, and pharmacology may be covered to some extent by the existing examinations, but it differs radically from that of technicians in clinical pathology in the absence of the common purpose that animates and binds together in a close fellowship all those whose work is directly concerned with disease. The lack of such a unifying influence no doubt explains the slow growth of professional consciousness among technicians whose work lies in science rather than medicine. If the desire for organisation is sufficiently strong, the best course might be to form an independent association of technicians in science, including not only physics, chemistry, and biology but also the medical sciences not directly concerned with disease.

SUMMARY

The training of medical technicians in Britain and America is described and discussed.

The main features of the American system are (1) a thorough study of pure science, followed by (2) a full-time one-year course covering the whole field of medical technology.

The main features of the British system are (1) concurrent study of science and technology for some years, and (2) specialisation in a single branch of technical work.

The importance of general education and systematic technical training for technicians is pointed out. The educational value of writing a thesis is emphasised, and it is suggested that suitably qualified technicians might work for the degree of M.SC.

Working in a foreign laboratory is of special value, and scholarships should be available to make this experience possible for technicians.

The institution of examinations for technicians in anatomy, physiology, and pharmacology is discussed. Their interests might be best provided for by an independent association of science technicians.

I am indebted for information to the American Medical Association, the Registry of Medical Technologists, and the Institute of Medical Laboratory Technology. I am grateful for criticism of the manuscript to Prof. S. L. Baker, Prof. I. L. Kandel, and Dr. F. A. Vick.

". . . consciseness and decision are, above all things, necessary with the sick. Let your thought expressed to them be concisely and decidedly expressed. What doubt and hesitation there may be in your own mind must never be communicated to theirs, not even (I would rather say especially not) in little things. Let your doubt be to yourself, your decision to them. People who think outside their heads, the whole process of whose thought appears, like Homer's, in the act of secretion, who tell everything that led them towards this conclusion and away from that, ought never to be with the sick. . . ." FLORENCE NIGHTINGALE, *The Art of Nursing*. Revised edition, London, 1946.

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Disabilities

21. DIABETES

DIABETES cannot be classed as a disability in the same category as the crippling illnesses magnificently overcome and vividly described by the contributors to this series; however, it is generally agreed that the diabetic carries weight in life's handicap, so here is my story.

I qualified in January, 1921. In February, 1925, when I was an assistant in a general practice, I became thirsty, and on testing my urine I found that the urinometer popped up to 1045 and Fehling's solution was reduced by one drop of urine. I consulted the "Chief" to whom I had been house-physician, and he said: "Four ounces of bread a day and no other starch." The doctor to whom I was assistant fell ill next day, and I had to carry the practice for a time. A new feeling of tiredness oppressed me; my thighs ached and I could hardly drag myself up stairs. The drastic reduction of starch made me feel empty and I used to come home wondering what on earth I could eat. I also had boils in my ears, and lost more than a stone in weight.

In June I went to an institution to be balanced with insulin. It is difficult now to realise how insulin was used in those early days when the principles of diet advocated by Allen were still in force; I was given a fast day and my daily diet was then gradually increased from nil to 2000 calories; when I left the hospital I was balanced on a prescribed diet of 34 grammes of carbohydrate, 166 g. of protein, and 190 g. of fat daily —about 2500 calories, with 5 units of insulin before breakfast and dinner. This was, of course, impossible to eat (you try getting through 3–4 oz. of butter with 1 oz. of bread to spread it on!), and the upshot was that I ate less calories, but I had protein bread and for a time weighed my food. I tested my urine once a week, and blood-sugar estimations were also done. I remained in full work, but gave up my subscription to a pack of beagles with which I used to run on Saturdays; this I now know was unnecessary.

All went well until January, 1927, when I contracted a streptococcal infection. The point of entry was a winter finger crack, and the cause of infection the daily dressing of a septic wound. I had remittent fever for weeks; infective axillary adenitis and finally pleurisy developed. Deep abscesses were opened and drained under anæsthesia and streptococcal serum produced a severe and interesting rigor. I seem by the notes to have tested my own urine; glycosuria and ketosis were heavy, and I increased the insulin gradually from 24 units in two doses a day to 60 units in three doses; the carbohydrate was kept very low (30–50 g.), and I struggled to take 6 oz. of brandy with water and bicarbonate of soda—a most nauseating drink. I survived this régime and had a series of hypoglycæmic attacks when I began to recover in March. I went for a cruise to Greece and returned to work in May.

At the beginning of this illness, before the infection localised, I thought that I should die because in hospital I had not seen or heard of a case of streptococcal septicæmia that recovered. I have always regarded the rest of my life as a second innings which has now lasted much longer than I could have expected.

Although my insulin needs were increased, I regained health and strength and led a full life. I was made a partner in the firm and as junior did my full share of night work and emergencies; I passed a higher examination and was appointed to the staff of a local hospital. I published several papers in the medical journals, and was concerned in the publication of two books. My diabetes did not hinder me in any way; for instance, I find a note in a diary that I came home by the midnight train after a long day in London, and gave an anæsthetic at 8.45 next morning, having bathed in the sea before breakfast. One Christmas night, having gone to bed at 1 A.M., I was called out at 2 A.M. and again at 5.45; my observation on this was: "Car difficult to start." I enjoyed holidays, walking, swimming, and climbing. My only real trouble was due to hypoglycæmic attacks which came in bouts after particularly anxious or strenuous periods. On holidays I usually averted reactions by taking less insulin and eating more but did not always succeed—as on one occasion after a long mountain climb I was overtaken near the end of the descent. I stumbled and staggered, fell, and would have gone to sleep among the rocks if I had not been helped down.

Looking back I think that in these years diabetes was more a social inconvenience than a disability. The restricted carbohydrates caused my friends to arrange a special meal when I went to dinner and the second dose of insulin was awkward when out for the day. The introduction of slow-acting insulin obviated this; and from 1938 to 1946 I used protamine zinc insulin and soluble insulin given separately but through the same needle before breakfast. I now use globin insulin and find the simplicity a great boon. Instead of fiddling about with two bottles, two measurements, and two needles, I have only one quick manœuvre, which is part of the routine of dressing and is much shorter and less troublesome than brushing one's teeth. I hardly feel the prick and the same needle lasts for months; I do not keep it in spirit but stand it attached to the syringe in a dry metal container. I do not even clean the cap of the insulin bottle. I have never had sore places, lumps, or abscesses, and a bruise is the signal for a new needle; I use the strength 80 units to the ml. and inject less than 1 ml. I have injected into the front and sides of the two thighs for nearly 24 years, yet it is impossible to detect the sign of a prick.

As regards diet, rationing and the gradual decrease in the food of the country have made the diabetic by comparison a highly fed person. The knowledge that carbohydrate makes no more demand on insulin than do protein and fat has been very slowly grasped and the diabetic rations are a last echo of pre-insulin notions. The allowance of butter and margarine (18 oz. a week) is quite ridiculous; 12 oz. of cheese is also too much except for heavy manual workers. The meat and milk however are very nice.

During the war, and to a less extent now, most cakes, scones, and buns in the shops contain no sugar and can be interchanged for bread in one's diet. I think it wise to avoid actual sugar and sweet food because it is so quickly absorbed into the blood and unbalances the blood-sugar, but this effect is less if it is eaten with or after other things. I now eat ordinary everyday food, avoiding only such things as treacle pudding. I have more milk in coffee and with porridge than the ordinary person, but the rest of my extra rations are shared with my family, the bulk going to the young and growing.

The war was a testing time for all civilian doctors, and the coast town where I practised went through many vicissitudes: I was now single-handed with a more specialist practice and my work rose in a gradual crescendo till I was relieved by doctors returning from the Forces. Air-raids, with night after night on duty at a first-aid post during the bombing of London, induced a continued sense of being on the alert. Daylight raids, tip-and-run bombing, and the whole gamut followed with an occasional rush of casualties. In addition to the ordinary hospital and civilian work there were first-aid lectures, Ministry of Labour medical boards, and additional consulting clinics for the Services, and I had more hospital beds. Above all, driving in the blackout was anxious and time-consuming, and the care of the

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car (the chauffeur having gone into munitions) was an added burden.

During these years I became unbalanced from time to time and had bouts of thirst and other diabetic symptoms alternating with hypoglycæmic reactions. I did not take any special steps beyond altering the insulin a little. Moreover I had two illnesses. The first, in January, 1943, was an irreducible hernia which had to be operated on as an emergency; this went without a hitch and I was at work again in three weeks. The second—jaundice—began a few months after the end of the war; it was severe and prolonged: I became weak and thin, losing rapidly about 1½ stone in weight. I had polyuria, diarrhœa, and a raging thirst. My usual diet was impossible; I had no appetite and revolted especially against fats. I ate lean meat, steamed fish, fruit, and cereals, drank gallons of water, soda-water, cider, and soft drinks, and increased the insulin gradually. This illness threatened to end my "second innings"; however, the "chance" was missed, and I have recovered.

* * *

I do not think I have suffered any ill from the diabetes itself; I have led and still lead a strenuous life and I can still enjoy hard exercise such as swimming. I weathered the illnesses recounted above, and my diabetes has not seriously deteriorated—indeed, I take less insulin now than I did in 1931 on two doses of soluble insulin. I have not yet developed any of the dreaded complications such as cataract, neuritis, or gangrene.

The disabilities are derived from the use or misuse of insulin, and sometimes hypoglycæmic reactions have landed me in awkward straits, even in jeopardy, and have caused alarm to my friends. I am not the stable type of diabetic and the margin is narrow. I do not now strive to keep my blood-sugar under the renal threshold, but even so I am sometimes caught. I do not think that the type of insulin matters. I had reactions on two doses of soluble insulin, I had them on P.Z.I. and S.I., sometimes at night; I have not had many and none severe on globin, but that may be want of occasion.

The symptoms in my case are generally confusion, stupidity going on to drowsiness, and a dead sleep, even coma. Things look different and when driving or walking I cannot recognise a familiar road. Sometimes I have the sense to eat sugar or sweets, sometimes I am overcome by sleepiness before I can do so. I have seen double and driven with one eye shut. I have also, I am told, had a convulsion. The more lurid incidents have had some obvious reason—e.g., after strenuous exercise. During a voyage we visited Nagasaki (of evil fame) and I separated from the party after a long swim, lost my way, and have no remembrance of getting on board—probably "brought in drunk." I awoke in my bunk at 11 P.M. some hours after the ship had sailed. During the war when on night duty at a first-aid post I crashed suddenly to the floor and awoke with alarmed faces round and honey in my hair. Apparently I had struggled too violently for intravenous glucose to be administered.

I have not often been overtaken when driving, though I spend many hours a day in the car. Occasionally I have found myself driving unsteadily and have stopped to eat sweets. More than once a passenger has brought me home, notably a nephew of 9 or 10 sitting beside me and handling the wheel, but I am generally alone and I had one reaction which might have brought me into the hands of the police. Towards the end of the attack of jaundice, when my liver was presumably depleted of glycogen, I was driving home late for tea. I remember seeing the name of a road about half a mile from home and hearing a bus driver shout at me. It seems I drew up opposite my own house and was found slumped over the wheel by a passing nurse who knew me.

I know the rules for avoiding or averting these attacks—lead a regular life; do not be late for meals; eat more and take less insulin when taking strenuous exercise; and carry sugar or sweets to eat at the first symptom. I attempt all these precautions, but so little does the disability affect me that I just do not remember it. The reactions worry my family and friends more than myself except for the sorrow and chagrin of giving so much trouble and alarm. They leave no after-effects and are quickly over. I am not afraid of having one when alone, because I am sure that the tendency is to recover. The only danger is that some well-intentioned person may give me a dose of insulin and close the chapter.

Medicine and the Law

An Assistant's Agreement

AN action has been brought, at the Lancaster Chancery Court, Manchester, by a former assistant against the practitioner who had employed him. The action was for the purpose of construing a clause in a service agreement, which restricted the plaintiff's activities as a medical practitioner after his association with the defendant had ceased.

The covenant in dispute stipulated that for seven years after the determination of his employment the assistant should not enter or carry on, either alone or in partnership, or act as an assistant to any persons carrying on, a practice as physician or general medical practitioner in the town concerned, or within a radius of 10 miles. The stipulation also restricted the assistant from practising as a hospital house-physician or house-surgeon or as the employee of the Government or the local authority. For every breach of these stipulations he was to pay £50 per day as damages.

Counsel for the defendant said that the question was one, not of construction, but of fact and law; he understood that the plaintiff had already begun to practise and had bought a surgery.

Counsel for the plaintiff said that he wished to know whether he could practise; the covenant was too vague and was unreasonable, and the wording was too wide. It was a master-and-servant case. The agreement was signed in May, 1945, when the defendant was in the Army. The plaintiff was to act at a salary of £960 a year during the principal's absence, and at £720 a year when the principal was able to participate.

In his judgment Sir Leonard Stone, the vice-chancellor, said that while the defendant was still away on military service his partner died and it became necessary to provide immediately for running the practice. So on May 24, 1945, the agreement was signed. Defendant agreed to employ plaintiff from Feb. 13, 1945, until such time as defendant was free to resume his civilian practice and subsequently unless such employment should be terminated "as hereinafter provided." The principal might determine the employment at any time by giving three months' notice. There was no provision in the agreement for its determination by the plaintiff. As had been pointed out by his counsel it appeared that as far as he was concerned it was an agreement for life. Nevertheless, there was nothing to prevent him breaking the agreement providing he was willing to pay damages. During the period after the partner's death, and before defendant returned, the plaintiff alone decided what was his daily round, and presumably it was he who kept the books at that time.

"Although I have no doubt the relationship between the plaintiff and defendant in law was that of employer and employee, the position which inevitably arises, by virtue of the circumstances I have already mentioned, placed the plaintiff in complete command of this practice for a period of over eight months," said the Vice-Chancellor. "I do not, therefore, approach this case as if the plaintiff was an assistant in the ordinary sense of the word—a young man who had

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perhaps only recently qualified and was gaining some practical experience. I have no hesitation in saying . . . that if the covenant is not one that is severable it is far too wide and therefore void as being against public policy, because the portion of it which restricts the plaintiff from doing the work of a hospital house physician or surgeon, or being an employee of the central Government or local authority, is quite unnecessary for the protection of the practice. On the other hand, it seems to me that if this covenant had merely been for a period of seven years after the determination of the employment, and that plaintiff should not carry on a partnership or act as an assistant in the town or within a radius of 10 miles, it would not have been too wide. Particularly is this so having regard to the fact that the plaintiff was left in sole charge, at a salary."

The second portion of the covenant, continued the Vice-Chancellor, dealt with something quite different—positions in which plaintiff would be in receipt of a salary. That meant a doctor in the employ of somebody as opposed to having the freedom of private practice. They came, in the Vice-Chancellor's opinion, within the definition of separate entities. The restrictive period governed them both. The covenant was severable, and that portion which restricted the practice within 10 miles was enforceable. "In other words," the Vice-Chancellor concluded, "the plaintiff can go to a local hospital and be a house-surgeon. It is somewhat in the nature of a drawn battle."

Public Health

Influenza

MEMORANDUM BY MEDICAL OFFICERS OF THE MINISTRY OF HEALTH

England and Wales have been singularly free from epidemic influenza in recent years, and apart from a few outbreaks due to virus A in residential communities at the beginning of 1947 there has been nothing to report since the mild epidemic due to virus B early in 1946. The first quarter of 1948 had the lowest figure ever recorded for deaths from influenza in the great towns.

So far there has been no indication of epidemic influenza in England and Wales this year, but reports have been received of an epidemic probably due to a variant of virus B in Italy, and recently of a mild type of influenza in France and Belgium. It is not yet known what virus type, if any, is involved in France or Belgium.

The importation of the disease into this country may be imminent, and it is therefore desirable to recapitulate briefly the main clinical features and the measures which may be useful in dealing with an epidemic.

Clinical Features.—The diagnosis of an individual case of true virus influenza is usually difficult and often impossible, and the occurrence of a number of similar cases at the same time is one of the most important leads to diagnosis. The onset is generally more sudden than that of a simple febrile catarrh, and the catarrhal symptoms are usually less marked at onset. Malaise and high fever with aching back and limbs are early symptoms, and headache, photophobia, and shivering are common; but the clinical features vary a little in different outbreaks. Influenza due to the known viruses is not in itself a dangerous disease, but its complications may be. During the pandemic of 1918–19 severe pneumonia with "heliotrope cyanosis" was a peculiarly deadly complication, but fortunately this syndrome has not been reported frequently since then.

Treatment.—Penicillin and the sulphonamides are ineffective in the treatment of the primary virus infection but may be of great value in the treatment of complications. Possibly prophylactic doses of sulphonamides may be of value in an institutional outbreak where secondary infections with a sulphonamide-sensitive organism are known to be occur ing.

Measures of Control.—In epidemic periods the virus is so widespread and so freely communicable from person to person that measures of control depend almost entirely on personal hygiene. The golden rule is that anyone who has headache, pains in the limbs, and fever should go to bed in a room by himself and stay there under medical care until he is better. In the hope of limiting the spread of infection visitors should be kept down to the minimum and only those who are looking after the patient should be admitted to the sickroom. Ordinary hygienic precautions, particularly with regard to discharges from the nasopharynx, should be observed (virus may be carried on the hands). Elaborate procedures of disinfection and fumigation have no advantages over soap-and-water, fresh air, and sunlight.

In recent epidemics in different parts of the world, variants of the two main types A and B have been reported, and against these the protective vaccine prepared against the main types have been ineffective. It is not yet known whether any existing vaccines are likely to have any value in protecting against the prevailing type, and in any case protective vaccination is impracticable as a general measure. It should be reserved for those who run special risks.

For the reasons already given, general measures have a limited value, but unnecessary overcrowding in ill-ventilated public halls should be avoided. Crowding of beds in hospitals to accommodate extra patients is to be especially avoided because of the dangers of spread of secondary infections.

SPREAD FROM THE CONTINENT

In London two people who arrived from Paris on Jan. 5 developed shivering and limb pains and felt extremely miserable on Jan. 6. Later they had headache, generalised aches, photophobia, a dry mouth, and some sore throat but relatively few symptoms pointing to respiratory infection; the same evening the temperature was 101°F or over. Both were beginning to improve 72 hours later. Virus has not yet been identified. There must have been numerous similar importations in the last week or two but nothing suggests that the disease is already spreading. Whilst dissemination of the virus is almost inevitable the outbreak need not necessarily reach epidemic proportions.

Inoculation and Vaccination of Travellers

Many countries insist that travellers before entering their territories should produce evidence of having been recently immunised against certain serious diseases, particularly smallpox and yellow fever. Inoculation against yellow fever is required of travellers who have come from or passed through an endemic yellow-fever area, when they arrive by air in a country where, although the disease does not exist, there may be conditions which permit of its development. In order to avoid detention or delays at the frontiers of countries requiring these measures, travellers must provide themselves with certificates of vaccination or inoculation on the prescribed international forms.

The Ministry of Health lately convened a meeting of experts, to consider the time which should elapse between smallpox vaccination and yellow-fever inoculation. The following conclusions were reached:

1. That yellow-fever inoculation should precede primary vaccination against smallpox.
2. That there should be an interval of at least 4 days between yellow-fever inoculation (when given first) and primary vaccination against smallpox (when given subsequently).
3. That if primary vaccination against smallpox is done first, there should be an interval of 21 days between vaccination and yellow-fever inoculation.
4. That where there is evidence of previous successful vaccination against smallpox, yellow-fever immunisation and revaccination may be carried out at the same session; but if time permits, yellow-fever immunisation should always precede revaccination by at least 4 days.

With regard to the age below which it is undesirable to carry out the commoner immunising procedures, the following recommendations were made:

Procedure	*Minimum Age*
Smallpox vaccination ..	No lower limit. Primary preferably before 6 months (optimum 3–4 months).
Yellow-fever inoculation	No lower limit. May if necessary be given in first week of life at full dose.
Typhoid-paratyphoid inoculation	Not under 1 year.
Cholera inoculation ..	Not under 1 year.
Typhus inoculation ..	Not under 1 year.

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In England Now

A Running Commentary by Peripatetic Correspondents

THE case of the small boy with his head through the railings, mentioned by my peripatetic colleague of Dec. 25, interests me because I have twice in a comparatively short time delivered an after-coming head on Westminster Bridge.

On the first occasion I was walking across the bridge from the south side when about half way over I saw a small crowd round two policemen and a small boy. The boy had put his head through one of the trefoil openings in the balustrade and one of the policemen was making a gallant effort to remove him. Having smeared the boy's head with grease, he was working with a file to enlarge the opening in the balustrade, while the little victim cried mournfully. It was clear to me what had happened, and as I learnt from the crowd that the little chap had been there over an hour I offered to release him. "Oh yes?" replied policeman no. 2. "We've got a lot of Smart Alecs in this crowd, but we're doing very well, so you needn't waste your time." His manner was rude and I didn't like it, so I continued on my way to the Strand. When I returned nearly an hour and a half later the crowd was still there and a perspiring bobby was still working away with his file, but the poor little victim was almost in a state of collapse. I felt very cross and pushed my way into the crowd, saying to the minions of the law, "Now look here, this nonsense has gone on long enough! Get out of the way and let me take the child out!" Thoroughly fed up with their labours, one of the policemen said, "All right. If you think you know so much about it have a go!" To put his head through the opening the boy had flexed his head with his chin almost down to his chest, then he had extended it to look at the boats so that his maximum vertico-mental diameter was greater than the opening in the trefoil. I made one of the policemen hold the child's shoulders close to the opening while I got my hand through and flexed his head, telling the policeman to draw him out while I kept the head flexed. He was disengaged quite easily and the whole operation had not taken thirty seconds. The crowd cheered and I could not help remarking. "If you'd let me do that when I first offered, the little chap would have looked much better and you wouldn't have looked so silly. Don't they teach you midwifery at your ambulance classes?"

The second case was exactly the same, but the small boy had only been hung up a matter of minutes and the policeman, for whom somebody had gone, had not arrived; so I got him out at once without trouble.

* * *

The other night I attended a B.M.A. lecture by a medical peer, and early next morning I had this dream.

I was waiting in an anteroom for the beginning of an examination for a postgraduate diploma which would entitle me to the letters F.F.M.—the Freedom Fellow in Medicine. There were other candidates but they were nebulous except for one who was my half-grown daughter Mary, aged 13½. I was filled with the usual pre-exam. feeling of total ignorance. It appeared that the exam. was to be taken in two parts, one in the forenoon and the other in the afternoon, and both question papers were already there. For the afternoon the main requirement appeared to be: "Dissect the . . . half of the axilla." The half to be dissected was specified, but whether it was anterior or posterior, upper or lower, inner or outer, I cannot now say. I was filled with misgivings. I was aware too that advantage might be taken of the hour luncheon interval to consult books of reference, since I knew the question. Then I realised that the examiner knew quite well that I could not do this, because into this interval must be packed all the work of my practice, the examination of compensation cases, the attendance at committee meetings. On a shelf below my table were half a dozen sets of papers, partly covering a similar number of open books of anatomical drawings, which were all the same. I displaced the papers from one sufficiently to see that brightly coloured blood-vessels were a prominent feature, and I knew that it was a dissected portion of the axilla. I wondered if it would help me if I uncovered one of these diagrams and brought it up to the top of the table. But I felt that if I was discovered I might be disqualified. I therefore turned my attention to the printed instructions for the examination. I read the first page through several times with a total lack of comprehension. Then the examiner entered. He was short, slightly bald, and had a close-cropped grey moustache. I had seen him somewhere very recently. . . .

Did I crib? Was I found out? Or am I a subconscious F.F.M.? Unless there is another instalment I shall never know, for at this point I was awakened by a maid who told me that Mrs. Chapman, who had gone to hospital yesterday for a version, was bleeding badly.

* * *

Comparative ophthalmology was never quite in my line (though I do happen to know that a camel's erythrocytes are oval and that xanthopterin from butterfly wings possesses hæmatopoietic activity in Chinook salmon); so when, a year or more ago, I met the two experts described by my peripatetic colleague of Jan. 1 (p. 37), any remarks anent rabbits' fundi would have left me cold. With me it was the absence of a Keeler that was my salvation, for, though I could see little enough with the instrument provided, the Great Man could not penetrate the murky depths at all, and a diagnosis of secondary optic atrophy, made in sheer desperation, was accepted without a murmur. I pride myself that I diagnosed the second expert unaided, though it was fortifying to have his concurring opinion. Since my fellow candidate made his acquaintance, however, I fear that, in addition to his studies in ophthalmology, he has taken to reading Freud and acquired an Œdipus complex, for his remarks about his father were anything but filial.

It is pleasant, when one contemplates the whitening bones of others who have followed in the same tracks, to think that these two gentlemen have helped at least two candidates to reach the promised land. But—can there be a darker side to their activities, an Evil Eye in fact? For I, too, am unmarried.

* * *

Do we all find that it is next door to impossible to escape from our profession while on holiday? I'm told that it is my own fault, that I have too sympathetic a manner, but the fact remains that I can't get away from medicine. The limit was reached last weekend at a houseparty of supposedly healthy people. Within the first twenty-four hours I was asked to treat a case of menorrhagia and another of amenorrhœa, to open a whitlow, to diet a 16-stoner, and to have a look at two sets of varicose veins. None of my fellow guests were out to get treatment on the cheap, but there was a doctor in the house and they couldn't resist "just asking." The climax came when the local vicar, in the midst of showing me over his lovely old church, started to tell me about his enlarged prostate. Next time I take a holiday I'll tell everyone I am a traveller in second-hand coffins and am not taking any more orders till after Christmas. That ought to choke them off; but will it? They'll probably ask whether my coffins are any better than those provided by Mr. Bevan in his new service, and there we'll be back at medical politics again.

* * *

I was condemned not long ago to lie for half an hour on the X-ray table of the hospital where in times past I was for many years a member of the staff. After taking one or two films the radiographer, a charming young lady but a stranger to me, departed to the far end of the room where she busied herself with other matters. Presently I needed her attention but was faced with the problem of how to address her. It certainly wouldn't do to call out "Nurse." "Miss," with its implications of a café, was dismissed too. Our local bus-conductresses address their fares indiscriminately as "dear" or "darling," sometimes even as "ducky," but none of these seemed appropriate from one in my position. No doubt she would have "answered to Hi or to any loud cry," but I sought for some less vulgar or distressful call. It was in vain. How *does* one signal to a radiographer?

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Letters to the Editor

NURSING EXPERIENCE FOR MEDICAL STUDENTS

SIR,—I welcome the letter last week by Mr. Carruthers and Mr. Richardson, for it calls attention to the necessity for giving the student some practical experience of the nursing and management of patients.

It is good for young men to dream dreams of fellowships and professorial chairs, but it is even better for them to realise the part that good nursing plays in the cure of disease and alleviation of discomfort. As a country doctor who has frequently to advise and help relatives to nurse patients in primitive and unsuitable surroundings, I am often relieved and—it must be confessed—secretly ashamed to see what improvement in the patient's condition takes place with an occasional visit from the district nurse.

Three weeks' experience in the wards will not make a nurse, but it may at least give the young physician a better understanding of how much he will in future be dependent on the skill and devotion to duty of the nursing profession.

Goulceby, near Louth, Lincs. E. C. CORDEAUX.

SIR,—Present-day nursing examinations seem to be turning their candidates into doctors. Perhaps the probationer might spend a few weeks as houseman to learn the "rudiments and difficulties" of his job.

My own sympathy and support goes to the students of the London Hospital, shortly to be handing out medicines and milk puddings under the critical eye of their ward-sisters. Not only has someone hit on the bright idea of turning them into junior pros (even though the rank is temporary and honorary) but you rap their spokesmen over the knuckles when they start complaining about it.

It just isn't worth it (even though future generations will incline their heads appreciatively and murmur, "you can tell he's a London man—knows all about bedpans"). If the student doesn't appreciate the niceties of nursing at the time, he won't be a houseman over a couple of weeks without realising all the difficulties the nurses have to put up with—the sister will spend most of her day telling him. The medical curriculum is already chaotically arranged and overburdened, so why inflict on the poor student, who has hardly time left to play rugger or Chopin according to taste, additional instruction in the work of related but obviously distinct hospital services? The signalman doesn't have to drive an occasional engine, the editor isn't expected to serve his time on the linotype, and nobody thinks the worse of Mr. Strachey for not doing his own cooking.

If the other hospitals follow your advice and take the London's lead, they might as well do the job properly. Every student should spend a month taking X rays, a few weeks preparing the hospital potatoes, undergo a course of floor-polishing under the head wardmaid, and have his stomach taken out to appreciate the rudiments and difficulties of being a patient.

General Hospital, Nottingham. GORDON OSTLERE.

SIR,—From personal experience I must disagree with your correspondents from the London Hospital medical college. During the war I was engaged for a time in full-time civilian nursing, and though there is no single thing which I can say is a valuable lesson learnt then, since commencing my clinical course I am more than ever sure that the ideal introduction to a medical career is a period of nursing.

Patients regard their dresser as a member of the medical staff, seen only for a few minutes at a time; and the relationship is very different from that with a member of the nursing staff where there must, at worst, be toleration on both sides for hours at a time—a valuable discipline which can only be assessed by those who have experienced it. Long experience is needed to judge accurately the condition of a patient "putting on his act" for the doctor—a fact quickly appreciated by the nurses, who see him without the temporary tonic of a visit from the medical staff. The comments of sisters on the remedial measures ordered by housemen suggest that many of the newly qualified are very ill-acquainted with the practical details of these operations, or with ward routine. It is a pity that any addition, however valuable, should be made to an already heavy curriculum; but as a final-year student, I consider that in the past two years I have done much of less value than nursing.

Charing Cross Hospital Medical School. J. A. EDDINGTON.

SIR,—I do not wish to express an opinion on the complaint of Mr. Carruthers and Mr. Richardson against having to undertake a spell of nursing duty. Arguments can be advanced on both sides.

I would only suggest that those who do not like the idea should, instead, spend at least three weeks in the wards as patients—preferably as sufferers from something which produces helplessness and malaise, or as subjects of a surgical operation.

This is a part of the medical student's education for which we can hardly provide deliberately; but, if anything could be more instructive than nursing, it is undoubtedly being nursed.

London, E.1. ALEX COMFORT.

OXYGEN THERAPY IN SHOCK

SIR,—Irrespective of its cause, shock is always attended by a slowing of the circulation and by unsatisfactory oxygenation throughout the body. During its passage through the tissues, the blood may give off 80% of its oxygen. Under such conditions the oxygen in the venous blood will be 20%, compared with the normal 60%, which is equivalent to a reduction of the partial pressure of the oxygen in the capillaries from about 40 to 15 mm. Hg. The consequence will be hypoxia in the tissues.

The view formerly held, that hypoxæmia gives rise to greater permeability of the capillaries, with a progressive loss of plasma into the tissues, has been disputed in the light of Nickerson's experiments.[1] It has been superseded by the observation that in hypoxia a vasodepressor substance with vasodilating properties,[2] is formed in the liver and muscle tissues. This substance, which is inactivated by normal liver tissue, is supposed to be the primary factor in the causation of irreversible shock.

The disturbance of metabolism in hypoxia gives rise to acidosis, which further impairs metabolism. Thus hypoxia initiates a vicious cycle. Together with its sequelæ, it is an increasing menace to the patient with shock.

The natural treatment of hypoxia is an increase of the oxygen content in the inspired air. This is obvious in cases with pulmonary damage which prevents the normal oxygen saturation of the blood in the lungs—i.e., arterial hypoxia. But also in the stagnant hypoxia of shock oxygen treatment is of greatest value.[3 4] In such cases, however, the deficiency of oxygen is liable to be overlooked, since it often does not manifest itself in cyanosis.

In stagnant hypoxia caused by shock the hæmoglobin of the blood, when it leaves the lungs, is saturated with oxygen to a normal extent—i.e., 97–98%. At the same time the blood contains a minor amount of oxygen in physically dissolved form, 0·26 ml. per 100 ml. If the patient is given pure oxygen, complete saturation of the hæmoglobin will be obtained—i.e., an increase of its oxygen carriage by merely a small percentage, or about 0·5 ml. per 100 ml. of blood. In addition, however, the amount of physically dissolved oxygen will increase by about 1·5 ml. Thus, when pure oxygen is inhaled, about 2 ml. more of oxygen is carried by 100 ml. of blood than when ordinary air is breathed. Under normal conditions 100 ml. of blood gives off about 6 ml. of oxygen during its passage through the tissues. The gain in oxygen-carriage when pure oxygen is inhaled—i.e., 2 ml.—therefore corresponds to a third of this normal requirement. A considerable surplus of oxygen is thus obtained.

1. Nickerson, J. L. *Amer. J. Physiol.* 1945, **144**, 429.
2. Schorr, E., Zweifach, B. W., Furchgott, K. F. *Science*, 1945, **102**, 489.
3. Schnedorf, J. G., Orr, T. G. *Surg. Gynec. Obstet.* 1941, **73**, 79, 495. Davis, H. A. *Arch. Surg.* 1941, **43**, 1.
4. Melton, G. *Lancet*, 1943, **i**, 481.

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The principal effect of oxygen therapy in shock is that the oxygen deficiency in the tissues is counteracted; but, probably, there is also a directly favourable effect on the disturbed fluid balance.

In healthy persons, after inhalation of 100% of oxygen for only a few minutes there is dilution of the blood, shown by a fall of the hæmatocrit and serum-protein levels. Hitzenberger and Molenaar [5] observed in 4 out of 5 persons, after the lapse of twenty minutes, an average increase of about 400 ml. in the circulating volume of blood, equivalent to an ordinary transfusion. This effect, however, is transient, and within an hour from the start of inhalation of the oxygen the original state of the fluid balance is restored. A transient slowing of the pulse-rate has likewise been observed.

Similar experiments in connexion with shock have not yet been made, but Melton [4] in treating shock with oxygen observed a slowing of the pulse-rate by more than 10 beats per min., and (in about half the patients) a rise of both systolic and diastolic blood-pressure by more than 20 mm. Hg.

How the oxygen produces this effect on the circulation has not been ascertained. For the present we must content ourselves with noting that the effect is very favourable and may possibly suffice to break the vicious cycle initiated by shock.

It may now be asked whether the patient with shock incurs any risk by inhaling pure oxygen.

Ever since oxygen was discovered it has been realised that high concentrations of the gas (over 60% at atmospheric pressure) in the inspired air entail for a healthy person toxic effects which after a time endanger life. At ordinary atmospheric pressure the lung tissue is damaged, and death from suffocation ensues: in 80–90% oxygen small animals, such as mice, guineapigs, and rabbits, die within two or three days. Extensive experiments have been made [6] and it has been supposed that oxygen, like phosgene and nitrous gases, directly irritates the lung tissue. Time-limits for the inhalation of pure oxygen have accordingly been fixed, differing according to different workers from 4 to 24 hours.

Thus the use of pure oxygen is still viewed with great respect in theory. But in practice the toxic effects have not been taken so seriously. Nevertheless no clinical case of oxygen toxicity has been observed. This can be partly explained by the fact that clinical methods of administration do not supply oxygen continuously at such high percentage as in experiments. But the main reason is that the misgivings have been based on false analogy. Observations on healthy people, do not necessarily apply to those who are hypoxæmic, and investigating this possibility I found [6] that animals rendered hypoxæmic by non-lethal pulmonary injuries survived in oxygen of high concentrations much longer than healthy controls. This result was surprising, since the opposite would have been expected if oxygen directly irritates the lungs. Injury to the lungs by oxygen in high concentration is evidently caused in some other, less direct, way—possibly through disturbance in the biochemical constitution of the blood. At any rate it has been made clear that inhalation of pure oxygen at atmospheric pressure, which for healthy people entails certain risks, does not endanger a patient with well-marked oxygen deficiency. Hence a patient with traumatic shock can inhale pure oxygen for an indefinite length of time, so long as the shock has not been abolished.

A reservation should perhaps be made in the case of pulmonary damage with hæmorrhagic tendency, as in blast injuries. Inasmuch as it has been shown—e.g., by von Euler and Liljestrand [7]—that oxygen tends to dilate the lung capillaries, it should be administered to such patients with caution, for fear of aggravating hæmorrhage.

As already indicated, oxygen should be administered on the same principle as any other drug—i.e., in a dosage regulated by the requirement. Every patient likely to have shock should receive oxygen prophylactically in a concentration not exceeding 60% at ordinary atmospheric pressure. A patient already affected by shock should be treated with 100% oxygen until the shock is abolished.

To sum up, oxygen is of great value in the treatment of shock, not only for the suppression of the hypoxia but also for its good effect on the circulation, similar to that of a transfusion. There is no time-limit for treatment with 100% oxygen: it can safely continue so long as the shock itself continues.

Örebro, Sweden. WILHELM T. L. OHLSSON.

5. Hitzenberger, A., Molenaar, H. *Klin. Wschr.* 1934, 13, 1599.
6. Ohlsson, W. T. L. *Acta. med. scand.* 1947, 128, suppl. 190.
7. von Euler, U. S., Liljestrand, G. *Acta physiol. scand.* 1946, 12, 301.

SURFACE-ACTIVE SUBSTANCES AND ANTIBIOTICS

SIR,—In the course of the M.R.C. report on laboratory tests of streptomycin therapy of tuberculosis (Nov. 27) the use of Dubos-Davis medium is described, and mention is made of Fisher's [1] observation on the effect of Tween 80 on the sensitivity of tubercle bacilli to streptomycin. This is not an isolated example of the effect of surface-active substances on the susceptibility of micro-organisms to antibiotics. Fisher quotes McCulloch: "This is probably due to an increase in the rate of diffusion of the bactericide into the bacterial cells, the velocity of diffusion being increased by the reduction of surface tension."

I have observed the apparent adjuvant action of sodium desoxycholate and of Teepol X, a synthetic detergent of the higher alkyl sulphate type, on the penicillin-sensitivity of *Proteus* and other gram-negative bacilli. These observations suggest that more than an increase in the rate of diffusion of the antibiotic is involved.

In the case of *Proteus*, for instance, an increased inhibitory zone may be observed in the cup-plate method to quite low concentrations of penicillin when the surface-active substance is incorporated in the medium in concentration insufficient alone to inhibit the growth of the organism. It is well known that many of these substances inhibit the swarming of *Proteus*,[2] but it is not this action which makes the organism appear more sensitive.

A plain agar cup plate, streaked with *Proteus* and containing 5–10 units of penicillin in the cup, will show after incubation no inhibition zone, or a zone of partial inhibition, the culture always growing to the margin of the cup. The phenomenon described by Gardner [3] is seen only on microscopy of the organism. The bacilli in the area near the cup exposed to sublethal concentrations of penicillin show extraordinary aberrant forms. For some distance from the cup margin the culture consists almost entirely of these filamentous, coiled and enlarged bacilli. These aberrant forms are a feature of most inhibition-zone plates, even with sensitive organisms; they are found at the edge of the inhibition zone as a band of varying width. When, however, 0·2% Teepol X is incorporated into the plain agar medium 5–10 units of penicillin in the cup will produce a well-defined zone of complete inhibition. This zone of complete inhibition is usually surrounded by a narrow zone of aberrant forms. In some experiments there has been an almost complete absence of these forms.

Further, if Teepol X is added to the penicillin cup on plain agar medium after incubation, a zone of lysis gradually appears round the cup. This lysis involves the aberrant form to a much greater degree than the normal form, and shows in the stained film as a granularity and a marked loss of staining power. It should be added that 50% Teepol X has a negligible inhibitory action on *Proteus* when tested alone in the cup plate.

It would thus appear that when *Proteus* is exposed to sublethal concentrations of penicillin the abnormal bacilli produced are more susceptible to the physical action of Teepol X than are normal forms. The result is an apparent increase in the sensitivity of the organism.

Only an analogy, of course, can be drawn between the action described and the Tween-80/streptomycin effect. The slow growth of tubercle bacilli would certainly favour a similar mode of action. It is worth noting that in Fisher's experiments with three resistant strains of tubercle bacilli, the addition of 0·2% albumin to his Tween-80 medium only partially reversed the effect of the Tween 80 and still resulted in an increased sensitivity

1. Fisher, M. W. *Amer. Rev. Tuberc.* 1948, 57, 58.
2. Lominski, I., Lendrum, A. C. *J. Path. Bact.* 1942, 54, 421.
3. Gardner, A. D. *Lancet*, 1945, i, 658.

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of at least a hundredfold, tenfold, and a thousandfold respectively.

The use of a Tween medium in measuring sensitivity of tubercle bacilli to streptomycin is questionable until these phenomena are further investigated.

Paddington Hospital, London, W.9. J. FIELDING.

*** An annotation on surface-active compounds in the chemotherapy of tuberculosis was included in our issue of Dec. 25 (p. 1019). In this article *para*-aminobenzoic acid was written in error for *para*-aminosalicylic acid, and (as we have already confessed) the words *in-vitro* were used when *in-vivo* was intended. —ED. L.

DIETARY FAT

SIR,—I must thank Dr. Walker for his detailed reply (Dec. 4) to my letter of Oct. 2.

On Sept. 18 he wrote that the daily fat intake during the war period in Switzerland was "40–50 g." and as Fleisch's [1] paper seems to have been variously interpreted it may be useful to state in more detail the figures derived from his graphs. The war lasted for nearly 6 years, but food rationing was introduced into Switzerland only in the autumn of 1942. Fleisch's graphs cover the period from 1943 to 1945. During these 3 years the average fat intake was 40 g. or less for 3 months, up to 45 g. for 10 months, and 45–50 g. for 14 months. The three groups of workers getting supplementary rations of 600–1800 calories are not included.

Dr. Walker agrees with me that in a properly balanced diet the absorption of the fat-soluble vitamins and of calcium and phosphorus depends on adequate fat intake, but he disputes its quantitative significance. He also quotes Wilson and Widdowson's [2] observations, that in people in the Central Provinces and Orissa consuming only 12 g. fat and 0·2 g. calcium daily, little or no rickets or osteomalacia are found. But Dr. Walker has omitted to mention the three other districts, observed by the same authors and quoted in the same table (p. 86), with apparently a similar diet to that in the Central Provinces and Orissa. In these three districts the daily calcium consumption varied from 0·3 to 0·7 g. and the fat from 19 to 28 g.; in spite of this distinctly higher calcium and fat intake one district had slight and the two other districts had very severe rickets and osteomalacia. Moreover, I should like to point out that according to the authors the freedom from rickets and osteomalacia in the Central Provinces and Orissa was due only to the plentiful supply of vitamin D from the sunshine (p. 89), and the significance of fat intake was not even discussed.

Dr. Walker appears also to object to my suggestion that adequate dietary fat has a sparing action on many of the B vitamins, and he quotes Elvehjem and Krehl's [3] recent review. Yet they observe that fat appears to have a sparing action on pantothenic acid, pyridoxine, nicotinic acid, choline, and very probably thiamine, whilst it seems to increase the riboflavine requirement (apparently through impairment with the biosynthesis). Neither did Dr. Walker favour the reference made to recent experiments which indicate that a mixed diet containing an adequate amount of fat confers great efficiency on the utilisation of food energy, and secures extra calories for work, growth, and storage.[4] Deuel and his colleagues [5] confirmed this in principle, and Elvehjem and Krehl [3] and also Drummond [6] appreciated this "fresh point of view concerning the value of fat in the diet." Dr. Walker, however, only notes from Forbes's study that altering the fat content of the diet of the growing albino rats from 10 to 30% resulted in an "energy retained" change from 456 to 460 calories daily—"a gain of less than 1%." "Supposing such findings are applicable to man, then at the 3000-calories level the gain would be less than 30 calories," says Dr. Walker. It would appear unnecessary to comment on a scientific practice which translates, even with the utmost caution, quantitative data from albino rats to human beings. Professor Forbes and his associates conducted a 70-day metabolism and body analysis experiment to determine the effects of differences in the fat content of isocaloric diets on the utilisation of food energy. At the end of ten weeks the average live-weights of the rats on isocaloric diets containing 2%, 5%, 10%, and 30% of fat were 220 g., 231 g., 235 g., and 239 g.; the nitrogen retained 6·11 g., 6·53 g., 6·55 g., and 6·71 g., and the energy retained 406, 440, 456, and 460 calories respectively. Is this "a gain of less than 1%?"

In the present state of our knowledge the minimum quantity of fat which should be present in the diet is not known,[7] but the small amount of available information indicates that there may be an optimum level. When large amounts of fat were added to the diet of dogs, increased erythrocyte destruction was observed,[8] and mice showed a lowered resistance to pneumococci after high-fat diet.[9] On the other hand, 1 of the 2 infants kept by von Groer [10] on fat-free diet, and 1 of 3 infants similarly dealt with by Holt [11] developed generalised eczema; Holt's case was cured by feeding fat. An adult, however, lived for 6 months on a practically fat-free diet and felt no ill effect apart from loss of weight, but the essential fatty-acid level in the serum lipids was considerably lowered.[12] The importance of these unsaturated fatty acids (linoleic, arachidonic, linolenic) for man is not quite clear yet, but markedly low levels have been found in certain eczematous conditions,[13] and some animal experiments suggest that the amount of essential fatty acids present in food might be a very important factor in a low-fat diet.[14]

A great deal of further research on the minimal amount of dietary fat is still required. Meanwhile it would be prudent not to overlook the non-caloric functions of dietary fat. Fat intake should not lightheartedly be reduced much below the normal established habits—even though the complicated metabolic processes are not as yet completely understood.

London, W.1. Z. A. LEITNER.

INDEPENDENCE AND RESEARCH

SIR,—It is interesting and significant to note that Dr. Waddington, in his reply to me in your issue of Jan. 1, uses very nearly the same terms as Stalin uses in his defence of his action in the affaire Lysenko. Prof. Sir Henry Dale, ex-president of the Royal Society, and Prof. Hermann Muller almost simultaneously resigned from honorary membership of the Moscow Academy of Sciences, explaining that their action was taken in protest against Lysenko's behaviour in relation with Vavilov, who would appear to have been liquidated as well as dismissed from his post by Lysenko.

Stalin claims that Russian scientists are unanimous in declaring that science cannot be divorced from politics, which is also Dr. Waddington's thesis. This doctrine, I submit, would be regarded in every civilised country as in itself denying to those who hold it any claim to be scientists. Happily, the doctrine inevitably entails such a setback in scientific achievement as to automatically discredit it. Expenditure on "politically directed research" has probably been larger in the Soviet Union since the revolution than in any other European State. Can Dr. Waddington point to any scientific discovery made by Russian scientists comparable with the advances in our own country in the same period of time—for example, the development of vaccine therapy, and the observation of the antimicrobic properties of penicillin opening up the whole field of the moulds, to cite only two examples from my own hospital in my own generation?

The Lysenko incident has evoked an extraordinary measure of attention all over the scientific world; it is in fact one of the most important demonstrations of Russian mentality, which keeps Russia out of step with nearly the whole civilised world.

House of Commons. E. GRAHAM-LITTLE.

1. Fleisch, A. *Schweiz. med. Wschr.* 1946, p. 889, fig. 4.
2. Wilson, D. C., Widdowson, E. M. *Indian med. Res. Mem.* 1942, no. 34.
3. Elvehjem, C. A., Krehl, W. H. *J. Amer. med. Ass.* 1947, **135**, 279.
4. Forbes, E. B., Swift, R. W., Elliot, R. F., James, W. H. *J. Nutrit.* 1946, **31**, 203, 213.
5. Deuel, H. J., Meserve, E. R., Straub, E., Hendrick, C., Scheer, B. T. *Ibid*, 1947, **33**, 569, 583.
6. Drummond, J. C. *J. R. Soc. Arts*, 1948, **96**, 569.
7. Leading article. *Lancet*, 1948, ii, 459.
8. Loewy, A., Freemen, L. W. Marchello, A., Johnston, V. *Amer. J. Physiol.* 1943, **138**, 230.
9. Sako, W. S. *J. Pediat.* 1942, **20**, 475.
10. von Groer, F. *Biochem. Z.* 1919, **97**, 311.
11. Holt, L. E., Tidwell, H. C., Kirk, C. M., Cross, D. M., Neale, S. *J. Pediat.* 1935, **6**, 427.
12. Brown, W. R., Hansen, A. E., Burr, G. O., McQuarrie, I. *J. Nutrit.* 1938, **16**, 511.
13. Brown, W. R., Hansen, A. E. *Proc. Soc. exp. Biol., N.Y.* 1937, **36**, 113. Finnerud, C. W., Kesler, R. L., Wiese, H. F. *Arch. Derm. Syph., Chicago.* 1941, **44**, 849.
14. Burr, G. O., Barnes, R. H. *Physiol. Rev.* **23**, 256.

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DIABETIC KETOSIS

SIR,—Dr. Black and Dr. Malins (Jan. 8) record and advocate a method of treating severe ketosis with *intravenous insulin* in vast doses—many hundreds of units—with the addition of saline. Obviously many of the cases they describe are not in diabetic coma and would come out of ketosis easily enough, in my experience, with small subcutaneous doses—often only 60–120 units spread over 12–24 hours.

Do they realise the action and fate of *intravenous* insulin? From its trial by Dr. Spencer in the insulin treatment of schizophrenics, which I partially suggested, it is clear that 5–10 units have a prompt effect, which disappears in 1–2 hours. If 20–100 units are given the action is slightly, but not greatly, increased and prolonged, and insulin seems to be rapidly destroyed when introduced into the blood-stream. And so it appears that vast doses of intravenous insulin amount in action to small evanescent ones.

This is fortunate in the treatment of ordinary degrees of ketosis because I think frequent large doses most dangerous, as perhaps recent correspondence in the *British Medical Journal* by Professor Dunlop, Dr. Oakley, myself, and others has shown. Dr. Black and Dr. Malins seem to me to be giving safe minimal active doses by the intravenous route. Most standard articles and books have for years advocated an initial intravenous dose to produce rapid initial action, to be followed by subcutaneous insulin. There is no evidence in their article that the above statement is wrong, but I am open-minded for correction.

Until then I think the smaller repeated subcutaneous dose of standard English procedure equally effective and easier in most circumstances, particularly in general practice by the non-specialised.

London, W.1. R. D. LAWRENCE.

TREATMENT OF URÆMIA BY INTESTINAL PERFUSION

SIR,—In 1947 Rogers et al.[1] reported that in three dogs experimentally rendered uræmic they had considerably reduced the amount of nitrogen in the blood by protracted intestinal perfusion with a saline solution whose composition they did not specify. In the 12–18 litres of perfusion fluid withdrawn they found 4–5 g. of non-protein nitrogen.

For some time we had been treating uræmia both by vividiffusion and by surgical drainage, but only in an experimental stage. So we decided to try intestinal perfusion, draining both the enteric juice and the bile simultaneously through a rubber tube.[2]

At first we used a double-lumen Miller-Abbott tube, but this proved inadequate because there was only a single opening for both intake and output of the perfusion fluid. Subsequently we used a three-lumen tube with a three-way mouthpiece: one for inflating the rubber balloon at the end of the tube, and the two others for separate intake and output of the perfusion fluid (fig. 1). In this way the perfusion could be done more rapidly, taking 6–8 hours. The perfusion fluid was injected with a syringe of 250 ml. capacity (fig. 2).

With this apparatus we treated three cases of mild uræmia in man by repeated intestinal perfusion, with good results. In severe uræmia vomiting makes our

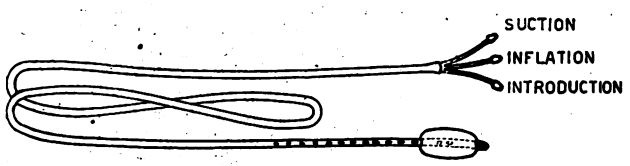

Fig. 1.

method impracticable. The portion of intestine chosen for perfusion was the upper jejunum to a distance of about 4 ft. from the teeth, so as to drain at the same time the bile, which in uræmia contains a large amount of urea.[3] The perfusion fluid was similar to one of the solutions used by Kolff[4] for hæmodialysis: sodium chloride 6 g., sodium bicarbonate 2 g., potassium chloride 0·4 g., and glucose 1·5–2 g. per litre. In the three cases treated by perfusing for 3–8 hours with 12–18 litres of this solution we extracted 1·8–2·7 g. of non-protein nitrogen, obtaining a remarkable diminution of uræmia—e.g., from 92 mg. of non-protein nitrogen per 100 ml. to 73 mg., from 108 to 83 mg., and from 122 to 84 mg.

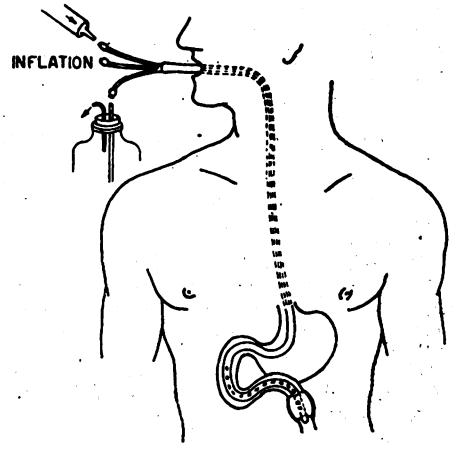

Fig. 2.

Since then we have obtained encouraging results in five other cases of nephritis and one of hepatorenal syndrome with icterus and uræmia. For the above-described tube we have substituted another three-lumen tube which allows the perfusion fluid to be introduced by gravity; and, to shorten the time taken in perfusion, we are experimenting with a compression-and-suction apparatus connected with the tube, with a view to using a much greater quantity of perfusion fluid.

Using the longer triple-lumen tube (supplied by the Fradagrada Company, Milan) we have perfused the intestine 90–100 cm. beyond the pylorus. In one case of nephrotoxic uræmia we established diuresis by perfusing the intestine repeatedly for 9 days. The results were as follows:

Day of treatment	Blood non-protein nitrogen (mg. per 100 ml.)		Perfusion fluid (litres)	Perfusion fluid non-protein nitrogen content (g.)
	Before	After		
1	136	111	16	2·38
2	139	82	29	4·92
4	167	115	24	3·79
6	121	94	10	2·42
8	144	102	16	3·20
9	122	99	8	1·78

The possibilities of this treatment of uræmia seem good both in cases of mild uræmia, the perfusion being repeated at intervals depending on the degree of retention of urea, and in acute uræmia involving only a moderate degree of retention. This method should also be effective in hepatorenal syndrome. The main advantage of this method is that it can be repeated many times, whereas such treatments as hæmodialysis and peritoneal dialysis cannot. Very little discomfort is caused to the patient; only the inflation of the balloon may cause a little pain.

If we succeed in perfusing more speedily with far larger amounts of fluid, we may perhaps obtain good results in severe uræmia also. Further, by varying the composition of the perfusion fluid and studying its physiological effect, we may be able to treat extrarenal hyperazotæmia successfully. Finally, we suggest the addition of secretin to the perfusion fluid for the sake of its stimulant effect on the liver, the pancreas, and the intestinal glands.

A. FIESCHI
M. BALDINI.

Pavia.

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SPECIALIST QUALIFICATIONS

SIR,—Having just read your very illuminating leading article of Jan. 8, may I suggest that, as an experiment, a single qualifying examination should be arranged for all medical students? It appears that there is scarcely a month in the year, save in the summer, when some body is not conducting one or other of its finals. Thus in a typical London school students are working for at least five possible qualifications. The curious thing is that these students all attend the same lectures and outpatient classes, go on the same ward rounds, and watch the same operations. I feel that one qualifying examination, held in London and in leading provincial cities not more than twice a year, would simplify academic medicine for both teachers and taught, and would make for a uniform standard of our art throughout the country.

Regarding specialists, there is a good deal of loose thinking. Thus in many provincial hospitals many of the surgeons have only the Conjoint diploma, and attempt major surgery really only within the purview of the F.R.C.S. grade. Again, many medical men call themselves psychiatrists who have never taken the D.P.M. or had any psychiatric training. In all specialist training it is vital for a sane balance to be struck between the academic and clinical aspects.

Long Grove Hospital, Epsom. J. B. GURNEY SMITH.

VEGANIN

SIR,—In his letter of Dec. 4 Mr. Warburton implies that 'Veganin' is a more potent analgesic, *weight for weight*, than tab. codeine co. *N.W.F.* Would Mr. Warburton care to quote experimental work in favour of this opinion?

Department of Materia Medica, The University, Glasgow. STANLEY ALSTEAD.

PREGNANCY TESTS WITH RANA ESCULENTA

SIR,—Your leading article of Dec. 18 refers to the use of various species of toad and frog for the pregnancy test devised by C. Galli Mainini. The South American toad, which he uses, *Bufo arenarum Hensel*, is not obtainable in Hungary. The common toad (*Bufo vulgaris*), though we have found it equally satisfactory for the purpose, cannot be readily procured here except in spring. Accordingly we have used the edible frog, *Rana esculenta*, and believe that as a test animal it is even better than the South American *Bufo arenarum Hensel* or the South African *Xenopus lævis*.

Method.—We inject into a male *Rana esculenta*, weighing more than 50 g., about 5 ml. of the urine to be tested. The injection is made subcutaneously into the lymph sac either abdominally or dorsally. Two hours later we take a few drops of urine with a pipette from the frog's cloaca and examine it under the microscope. If the woman's urine contains an increased amount of gonadotrophic hormone, spermatozoa will be found in the frog's urine. For each test we use two animals. If a very early pregnancy is suspected, it is advisable to inject one of the frogs with a larger quantity of urine. The reaction is taken to be positive even if the urine of only one of the frogs contains spermatozoa. The spermatozoa disappear from the frog's urine 3 or 4 days later, after which time the frog can be used again. Usually we give them a week's rest. Inexperienced persons may mistake the lively moving spermatozoa for protozoa usually found in the cloaca.

Results.—Of 610 pregnancy tests done in this way since last spring, 256 were positive and 344 negative. In 10 cases the frogs were killed by the toxicity of the urine injected. The clinical course could be followed in 420 cases, and the results may be summarised as follows:

	Positive	*Negative*	*Animals died*	*Total*
Reactions	256	344	10	610
Reactions controlled clinically	218	202	—	420
Reactions controlled and found correct	218	198	—	416
Reactions controlled and found incorrect	0	4	—	4

It will be seen that in the verified cases we had only 4 false results, and no false positive reactions. The number of correct results was probably higher than the figures suggest: some gynæcologists who received our reports did not trouble to write to confirm their accuracy.

These results correspond with those reported by Dr. Galli Mainini (personal communication), as having been obtained in 6956 tests made by himself and by other workers using *Bufo arenarum*. They did not obtain a single false positive, and in cases of proved pregnancy the results were more than 98% correct. In 1617 cases they compared the bufo test with the Friedman reaction and found the toad test wrong in 17 cases and Friedman's wrong in 40.

In about a third of the cases, our results were compared with those of the Aschheim-Zondek reaction, and in all of 5 cases which differed the frog test proved correct.

In our positive results 37% of the women were less than a month pregnant, 47% less than two months, and only 16% more than two months. We always obtained negative results in cases of lactation and of climacteric amenorrhœa.

Specificity.—We made our experiments on frogs caught in spring, summer, and autumn. We never observed spontaneous release of spermatozoa; nor were spermatozoa emitted after the administration of ovarian, follicular, or testicular hormones. Galli Mainini has tried different hormones but not obtained any positive results apart from the administration of gonadotrophic hormone.

Sensitivity.—The sensitivity of *Rana esculenta* is about thrice that of *Bufo arenarum*, which requires about 40 units of gonadotrophic hormone to give a positive result, whereas *Rana esculenta* gives a positive result with only 10–12 units. We are trying to increase the sensitivity of the reaction—purely from an academic point of view, because in practice too great a sensitivity may lead to false positives.

Advantages.—The exactness and specificity of this reaction make this test as sure as any other known pregnancy test. A great advantage of it is its quickness: it can be read after two hours, and in cases of two months' pregnancy even in one hour. The speed of this reaction is especially valuable in cases of ectopic pregnancy. The test is very simple and economical. The result is clear-cut—the presence or absence of spermatozoa. Further, *Rana esculenta* is easily obtained and easily kept for months, not requiring any special treatment, and one frog can be used several times.

Mode of Action.—According to our experiments the chorion-gonadotrophic hormone acts directly on the testes without the intervention of the pituitary gland: the reaction takes place equally well in decapitated frogs.

I. BACH
I. SZMUK
L. RÓBERT
B. KLINGER.

OTI Hospital, Budapest.

DODGEMS

SIR,—The history of motor transport abounds with laws and suggestions for general speed-limits, ranging from 4 m.p.h. in this country before 1896 up to about 50 m.p.h. in recent years. Dr. Fletcher Woodward, who was quoted in your annotation of Dec. 25, is continuing the tradition; he puts the *ultra quam nemo* at 55 m.p.h. Yet a little thought shows that all general speed-limits are absurd. No man can say that 56 m.p.h. is dangerous even on a given piece of road at a given time without considering and knowing well a given car and driver; what is highly dangerous for a novice in an Austin Seven may be safe for a really skilled driver in a Bentley. Some drivers, trained in racing, have with discretion used speeds of over 100 m.p.h. without accident to themselves or anyone else; I do not say "without danger," for all life is a matter of calculated risks.

Household accidents kill and injure more people than road accidents, yet nobody calls kettles and staircases "lethal and crippling agents." Information from the Royal Society for the Prevention of Accidents shows that in 1945 accidental deaths were as follows: roads, 5256; railways, 495; mines and factories, 1401; remainder, 10,434, of which over 8000 were home accidents.

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Dr. Woodward seems to be concerned only with private cars and their drivers. Here we have hardly begun to train road-users and to make safer roads, since authority has always found it easier and cheaper to harass the citizen than to do the job the citizen pays for. Raids on the Road Fund and a thousand other sins of omission and commission can be cited. Before the war experiments in Edinburgh with police patrols specially trained to provide all-round experience resulted in a steady and considerable drop in road accidents over several years. This system of warning *and teaching* road offenders of all groups on the scenes of their offences, and prosecuting only in serious cases, probably paid for itself in cost which was spared the courts. It is a proved remedy, and that it has never been applied over a wider area I can only put down to the reason given above. We shall have to come to it one day, and attempts to pin all blame on one kind of road user can only postpone that day.

Chester Beatty Research Institute, London, S.W.3. D. J. CAMPBELL.

TOXOPLASMOSIS

SIR,—Your leading article of Dec. 11 states that no strain of *Toxoplasma* propagated in suitable animals exists in Britain. This is not correct as we maintain a strain obtained from America in this department and have been able to supply the strain to other workers on request.

H. E. SHORTT
Director, Department of Parasitology.
London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

***Professor Beattie has already pointed out (Dec. 18) that similar arrangements have been made at Sheffield; and the same, we are informed, is true of several other centres. We regret the mistake.—ED. L.

NO ROOM AT THE HOSPITAL

SIR,—Those responsible for the administration of our London teaching hospitals have read with interest your leading article of Dec. 18 and the subsequent correspondence. We have noted with particular interest recommendations that the domiciliary treatment of the chronic sick should be developed and encouraged.

There are too many patients in our teaching hospitals suffering from malignant disease, paralysis, heart conditions, &c., who, having been admitted and investigated for an acute symptom, are found to be beyond permanent relief and in need of weeks or months of constant medical and nursing attendance. I have not, however, noticed any practical proposals for the accommodation of these cases, which freeze substantial numbers of beds in our hospitals. This blocking of beds has led to the exclusion of patients—many with acute illness—needing the elaborate investigation and treatment which may be available only at the large teaching hospitals.

The remarkable progress in medical science in the past forty years has led to the prolonging of life, but there has been no appreciable increase in the provision of beds for the irrecoverable or dying patients. Accommodation reserved for such cases before the war at the London County Council hospitals is now no longer available; so we are unable to admit from our surgeries, or in response to calls from the Emergency Bed Service, many whose acute condition needs inpatient treatment, and also patients needing early admission from our outpatient departments who are suffering hardship by delay.

We have to remember that for the teaching of students our teaching hospitals must be properly balanced in regard to the type of case. At the moment far too many beds are occupied by chronic sick and by ill and irrecoverable patients. The experience of the teaching hospitals suggests that urgent attention should be directed to the following matters in the order given: (1) the provision of accommodation for the post-acute irrecoverable and dying patients for whom constant medical and nursing attendance is needed; (2) the provision of additional sanatorium accommodation; and (3) the development of domiciliary treatment for the chronic sick.

Additional hospital beds will not be available for some years, and even when the time comes for building new hospitals economy in the use of nurses is essential. Let us be sure, therefore, that we get the "right patient in the right bed." We must not waste the beds in hospitals possessing full staffs of skilled doctors and nurses. We must see that the chronic and post-acute cases are found comfortable and suitable accommodation in hospitals and homes where a less generous proportion of skilled nursing is permissible.

London, S.W.1. HOUSE GOVERNOR.

THE CAUSE OF DIABETES

SIR,—In the Royal Society of Medicine's discussion on Dec. 14 Prof. H. P. Himsworth drew attention to the fall in the incidence of diabetes, and in diabetic mortality, observed in this country during periods of food-rationing, suggesting that food restriction, particularly of fat, might be responsible. Your leading article of Dec. 25 drew attention to the importance of his observations. My own information on the state of the German diabetic, who has been subjected to extreme food shortage, supports Professor Himsworth's conclusions.

Last June I visited the principal towns in the British zone of Germany and the British sector of Berlin, as a member of a delegation representing the council of the Pharmaceutical Society of Great Britain, to investigate, among other things, the question of medical supplies to these areas. I took particular interest in the insulin position, and visited many hospitals and clinics for this purpose. It was quite clear at that time that insulin supplies in the British zone, and particularly in the British sector of Berlin were insufficient for the needs of the diabetic population. Prof. F. Bertram, of Hamburg, stated that his supplies allowed an average of 26 units of insulin per diabetic, the estimated optimum requirement for all purposes being 40–46 units. At the Diabetic Centre in Berlin, which supplies diabetics from all four sectors with insulin, and had some 8000 diabetics on the books, Dr. H. Bernhard stated that 4000 patients, many of whom needed insulin, received none, and no patient received his optimum insulin dosage. Insufficient insulin dosage, as shown by glycosuria and high blood-sugars, was repeatedly checked by me from inspection of ward charts and outpatient record cards.

In spite of this considerable insulin shortage all physicians dealing with diabetics were of the decided opinion that the incidence of coma and ketosis, except at times of complete insulin lack, has fallen greatly since the war, even in the presence of high blood-sugars and septic complications. During my inspection of diabetic wards I was continually impressed by the absence of ketosis in patients with serious complications such as pneumonia and infected gangrene, with very high blood-sugars. I saw no obese diabetics. Dr. Bertram was of the opinion that the *diabetic* state of the average diabetic had considerably improved since the war.

The reason for these facts, in the opinion of the German physicians, was the very low-fat and low-calorie diet imposed upon the German diabetic since the war. The average diet obtained by Dr. Bertram's patients at the Langehorn Hospital, Hamburg, was 250 g. carbohydrate, 70 g. protein (20 g. of which was animal), and 50 g. fat, yielding 1730 calories; and by Dr. Feiler's patients at the Hoengatow Hospital, Berlin, 300 g. carbohydrate, 40–45 g. protein (animal and vegetable), and 35 g. fat, yielding 1700 calories. Patients were prescribed no diet, but ate such food as they could obtain.

The improvement in the average diabetic state was, however, more than offset by the greatly diminished resistance of the patient to infection, owing to undernourishment. Skin infections, gangrene, and perforating ulcers had all increased. Pulmonary tuberculosis running a rapidly fatal course was common, and according to Professor Bertram pneumonia mortality had risen from 3 to 10% in the post-war period, with prolonged pyrexia and delayed resolution a frequent complication.

A statistical analysis of these general impressions would, I am sure, reveal many interesting facts concerning the influence of diet on the incidence, morbidity, and mortality of diabetes, and one hopes that reports on these lines will eventually be produced by the German physicians.

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From recent information received from both the British zone and the British sector of Berlin, I understand that insulin supplies have considerably improved during recent months.

St. Alfege's Hospital, London, S.E.10. B. A. YOUNG.

OSTEOPATHY

SIR,—History shows us that at times of great national crises, such as follow on a war and the dissolution of an empire, new and fancy religious cults and therapies are apt to develop. It is not surprising therefore that osteopaths should try to emerge from the odium in which they sank as a result of the Select Committee of the House of Lords in 1935. No doubt they have been encouraged by the publicity given to the retropulsed intervertebral disc, and by the war-time resurgence of physiotherapy with its pseudo-scientific and unsubstantiated claims. What is surprising is that a reputable medical journal should encourage the osteopaths.

I do not think, Sir, that you have any justification for your action merely because medically qualified osteopaths are concerned. When all is said and done, our profession has always had its misguided indealists, its fools, and even its rogues, and there has never been any difficulty in obtaining the support of medical men for all kinds of scatterbrained ideas—whether to support anti-vivisection, to testify to the efficacy of Abram's Magical Diagnostic Black Box, or to further the interests of osteopathy. I cannot see the necessity for any medical man, who has presumably received a scientific training, to visit the London College of Osteopathy, when all that is necessary is to read their textbooks. Anybody who has read any textbooks on osteopathy, such as *Osteopathy, Research and Practice* by its founder, A. T. Still, the *New Healing* by W. H. Streeter, published by Methuen, or the *Scientific Basis of Osteopathy* as presented by Dr. W. H. Kelman MacDonald, to the Select Committee of the House of Lords and published by the Stationery Office (1935), can fail to see the ridiculous nature of the claims of the osteopaths.

Osteopathy is not, as your leader and the report of Batchelor and Cohen in your issue of Dec. 25 seem to suggest, just another term for manipulative surgery, but a claim for a common ætiology and a common therapy for all diseases, whether inflammatory, infectious, traumatic, or neoplastic. I wonder if you or your readers realise that osteopathy was founded by an American unqualified medical practitioner who, at ten o'clock on the 22nd day of June, 1874, had a divine revelation, and that God, whom he claimed to be the father of osteopathy, handed him two tablets of gold, on which were inscribed the principles of osteopathy. These principles were :

1. That the body is self-sufficient, manufacturing its own remedies, and that no drugs are necessary ;

2. "The rule of the artery is absolute, universal, and it must be unobstructed or disease will result." (He meant by this, for example, that obstruction in the arteries of the cervical vertebræ resulted in diphtheria, hyperthyroidism, &c.)

3. "That all diseases are merely effects, the cause being a partial or complete failure of the nerves to conduct the fluids of life." Still thought that the nerves were hollow. "We shall see," he said, "that the nerves drink crude blood fresh from the capillary arteries, refine, finish and apply it to form muscle, nerve, vein, artery, bone, brain, and kidney," and that "the womb-like cells of the nervous system in which atoms of living flesh are formed by nerve processes that act to give life, motion and form to muscles, organs, &c."

Still himself believed that the obstruction to the artery and the vital juices flowing down the nerves, occurred largely at the hip-joint but also at the ribs, sternum, and the vertebræ. With the growth of radiology this position is completely untenable by modern osteopaths, though they still pay lip-service to it in their textbooks and in their journal. The modern conception is that there is an "osteopathic lesion," which some people claim to have seen in X rays and at post mortems ; others say that it cannot be demonstrated by these methods, but they all claim that they can feel it with their fingers. Nowadays also they are prepared to accept the giving of drugs and the performance of operations, and even are prepared to admit the rôle of bacteria and viruses ; but they say that anybody will develop, for example, a gastric ulcer or smallpox if he is not "osteopathically sound," and he will not make a satisfactory recovery unless his back has been manipulated to relieve this "osteopathic lesion." They claim that it is no use to give insulin to the diabetic, or liver extract to the patient with pernicious anæmia, unless his back is manipulated at the same time. Surely, Sir, it would be a matter of absolute simplicity for an osteopath to manipulate a back and then to demonstrate a reticulocyte response or a decrease in the blood-sugar. Or is this too scientific and blasphemous for one who carries on his art because of divine revelation, and that, mark you, inscribed on tablets of gold, unlike the tablets of stone with which Moses had to be content.

This letter is long, but if I were to refer to all the idiocies, quackeries, and dangers of osteopathy to the patient, I should require much more than an entire issue of your journal. I feel that I, as an orthopædic surgeon, must protest against your trying to foist this child of a madman's brain on orthopædics, and to suggest that orthopædic surgeons should try osteopathic manipulations in their outpatients' departments. My quarrel, Sir, is with you, and not with the osteopaths, medically qualified or otherwise. I am not concerned, as Charnley is in your issue of Jan. 1, as to the motives for a medical man becoming an osteopath. I am not concerned with the question of whether he is a misguided idealist, or a fool, or a psychopathic personality who, because he has not been given the position in the medical world which he considers he deserves, has turned to osteopathy to attack the profession—possibly as an alternative to belittling it in novels.

SIDNEY PAPPWORTH.

Orthopædic and Accident Department,
City General Hospital, Sheffield.

*** The existence of osteopathy is a fact, which, like other facts, the medical profession should face. Mr. Pappworth has taken the trouble to study the subject in books, and we have taken the trouble to discover what, in 1948, the London College of Osteopathy was actually doing. Though osteopathic theory is largely, if not entirely, worthless, the disorders of the vertebral column, and their relation to symptoms, are undoubtedly important ; and it is possible that some osteopaths, by concentrating their attention on the manipulative treatment of these disorders, have developed useful techniques or manipulative tricks. We cannot withhold a measure of encouragement from any group of medically qualified people who want to demonstrate their technique to their colleagues in an open way ; for in such circumstances truth is bound to prevail. The real danger from osteopathy is that it will continue to thrive as a mystical underground movement which the public will continue to cherish because they believe that orthodox doctors are unwilling even to hear what unorthodox ones have to say.—ED. L.

THE NICOTINIC-ACID TOLERANCE TEST IN INFANTS

SIR,—Erdei has claimed[1] that the nicotinic-acid tolerance test devised by him gives useful information on liver function. Since sensitive tests presenting less technical difficulties than the ones currently used are of great importance in the management of infantile diseases, we decided to check its reliability in spite of doubts about its theoretical foundations.

The test was performed on 179 infants, of whom 25 were healthy and 154 had various diseases. The infants were given by mouth, an hour or two after a meal, a first dose of 25 mg. or, if they weighed more than 5 kg., 50 mg. of nicotinic acid ('Vitaplex N Chinoin') dissolved in water. If there was no response, 25 mg. was given every 10 min. until flushing of the skin was observed. The reaction, especially if it developed after not more than three doses, was in most instances unmistakable. In view of the great differences in weight of the infants, it was found advantageous to express the results by the fraction : Nicotinic-acid tolerance (N.T.) = mg. of nicotinic acid administered ÷ body-weight in kg.

1. Erdei, A. *Brit. med. J.* 1947, 1, 822 ; *Lancet*, 1948, 1, 368.

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The 25 controls were all healthy and developing well. The N.T. exceeded 15 in none of them; the lowest figure recorded was 8, the mean 10·5. Repeated tests gave strikingly uniform results even if made at intervals of several weeks. In view of Spear's statement [2] that the result depends on the time elapsed since a meal, 7 infants with either normal or raised N.T. were tested on two successive days, after fasting for eight hours on the first, and an hour after a regular meal on the second, day. No differences were observed between the two values. If, however, the second test was made not more than 20 min. after a meal, the N.T. was increased by 20–30% in a third of the cases.

Of the 154 sick infants 28 had a N.T. above 20. They were all in a more or less severe condition, 11 showing acute symptoms of toxicosis due to various infections, or were just recovering from a similar state. One of these gave the highest N.T. observed—44. In 7 infants there were purulent conditions, such as mastoiditis, disseminated abscesses of the lungs, and empyema, and the rest were, besides cases of enteric infections, a case of congenital syphilis with pneumonia, a decompensated Eisenmenger syndrome, and two prematurely born infants with complete failure to develop (one of them, a female baby of 6 months, weighed 2 kg.).

It must be emphasised that all the infants in this group either presented grave acute symptoms or were in a chronic decompensated state. All the infants who showed a N.T. of 15–20 were in a far better condition than those just mentioned. Most of them had upper respiratory infections or mild purulent processes, such as cystopyelitis, or had almost recovered from diseases like those in which a N.T. of more than 20 was found.

It is evident that the real usefulness of the test is determined by the sensitivity with which it can follow changes in the condition of a disease. In infants this is especially important in toxic states. The results were rather encouraging. For instance, in an infant admitted with a common cold the N.T. was 11; a few days later, when she developed toxic symptoms, the N.T. rose to 21, and then gradually decreased to 12 with amelioration of the condition. In 12 infants at the height of toxicosis the N.T. was between 20 and 40. In all the 11 cases observed just after the acute symptoms had ceased the N.T. was still found at the highest level. It took from one to three weeks before the values returned to normal (below 15). The decrease of N.T. seemed to coincide with the end of the so-called reparation period—i.e., it took place when the appetite returned and the weight began to increase. There were cases of infection with malaria and *Salmonella paratyphi* B which, at the beginning of the disease, showed a normal N.T. Later, however, and apparently parallel to the aggravation of the clinical state, the N.T. gradually rose to above 20.

Hanger's cephalin-flocculation test was serially performed in several of the above cases. There seemed to be a fairly strict parallelism between the two tests, an N.T. above 20 corresponding to a +++ or ++++ positive flocculation, whereas a normal N.T. coincided with negative Hanger reactions.

In 3 infants with chronic mastoiditis and N.T. 15–18 there was a steep rise to 24 and 29 after operation and then a gradual decrease to nearly normal within a few days. The same sudden rise and fall of the N.T. was observed in an otherwise healthy infant after operation for cleft palate. In all the cases in which the N.T. was found increased, its level did not change unless the state of the patient changed. The observations were too few to decide whether definite conclusions could be drawn from the height of the N.T. about the severity of the illness.

It is difficult to assess the results and to establish the usefulness of the test without the knowledge of its exact mechanism. Erdei's explanation seems rather questionable, especially since it has been shown [3] that the aminisation of nicotinic acid does not take place in the liver. Besides, it is not only the excess of nicotinic acid that reaches the circulation, and the promptness with which the reddening of the skin appears after an adequate single dose makes it improbable that the aminising capacity of any organ could have been exhausted so soon. The same points were also raised by Ellinger [4] in his criticism of the test, with the assumption that it is not the quantity of nicotinic acid in excess of the aminising capacity that is responsible for the vasodilation; but the general vasomotor lability might be decreased in certain liver diseases. Such a correlation is not yet known to exist; indeed, it is unlikely, because sensitivity to histamine is not increased in several conditions in which high N.T. values were observed.

Many experiments will apparently be needed before the mechanism of the reaction finally becomes clear, and it would lead too far to discuss all the possibilities in advance. Still, whatever the biochemical foundation of the test may be, our observations have uniformly shown that the N.T. was definitely increased whenever clinical signs of disturbed intermediary metabolism appeared. The results seem to confirm Erdei's supposition—that the N.T. depends on liver function, or, more strictly, on protein katabolism. This is made even more likely by the parallelism to the cephalin-flocculation test; by the N.T. in diseases which, like malaria or salmonella infection, are known to lead to late hepatic damage; and by the increase in N.T. after operation, which phenomenon can hardly be explained by a factor other than the increased katabolism of proteins.

1st Department of Pædiatrics, University of Budapest.

P. V. VÉGHELYI
A. SASS-KORTSÁK.

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4. Ellinger, P. *Lancet*, 1948, i, 539.

Obituary

CLAYTON ARBUTHNOT LANE

M.D. LOND.

Colonel Clayton Lane has an assured place in the history of tropical medicine as a pioneer in methods of mass diagnosis and treatment of ancylostomiasis. Few could rival him in his experience of helminth infections or in the practical value of his contribution to his specialty.

He qualified from St. Mary's Hospital in 1893, taking his M.D. two years later. After holding a demonstratorship in physiology and house-appointments at St. Mary's he joined the Indian Medical Service, and soon became engrossed in the study of helminthology. It was characteristic of his precision and sense of responsibility to insist on the need to diagnose infection in the individual before embarking on the treatment of a community with drugs which were not devoid of danger, and his interest in diagnosis led him to devise the centrifuge which bears his name. He applied these principles and his direct centrifugal floatation (D.C.F.) method of diagnosis when in 1915, in the tea gardens of Darjeeling, he organised a mass treatment of ancylostomiasis based on accurate diagnosis.

[Harry P. Rider

Though this work was his chief contribution to helminthology, he also made important observations on periodicity in filarial infection. "Here," writes R. C., "he broke new ground with vigour and originality. Abandoning the universally accepted explanation that the embryos lodged during the day in the organs and entered the peripheral circulation at night, he put forward the alternative hypothesis that the reason for periodicity might be the periodic discharge of embryos from the ovaries of the female filarial worm. He was also one of the first to point out how much new precise knowledge about malaria might be obtained from the therapeutic use of this disease in the treatment of general paralysis." He had his critics as well as his supporters, for he was apt to be carried away by his enthusiasms. He continued, for instance, to maintain that thymol was the best agent against hookworm, though most workers have discarded

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the drug. But even where his conclusions did not find general acceptance the arguments he brought forward were respected.

Lane retired early from the I.M.S., but he was soon at work again in this country at the Albert Dock Hospital, where, with a grant from the Royal Society, he continued to develop and perfect his D.C.F. technique. Of his long and patient labours there a colleague writes: "His valuable but unspectacular addition to accurate tropical medicine was appropriate to his personality, for he had a silent capacity for taking pains in persistent, undeviating pursuit of accuracy. His floatation technique was widely adopted and sometimes 'simplified.' Then his work was enlivened by his pursuit and exposure of these deviations, and his prose, usually indirect and modest, became something acid—and good reading."

During his retirement he also gathered together his long studies and first-hand experience of hookworm disease in an authoritative volume, *Hookworm Infections*, which was published in 1932 and is still a standard work. His critical summary of the literature dealing with housing and malaria, prepared for the League of Nations, had already appeared in the previous year. For many years he edited the helminthology section of the *Tropical Diseases Bulletin*, and his abstracts, always written in Basic English, showed how a vocabulary of only 850 words, apart from technical terms, can lend itself to incisiveness and simplicity. For the *Bulletin* he wrote many papers on helminthological subjects, some purely systematic, and other bionomical, such as his studies on thigmotaxis in ancylostome larvæ. During his hon. secretaryship of the Royal Society of Tropical Medicine and Hygiene, which he also served as vice-president, he took charge of the *Transactions* and did much to give them their present format, character, and high standing. Only four years ago, in our own columns, to which over the years he had made many welcome contributions both signed and unsigned, he gave a masterly summary of threadworm infections.

When failing health finally enjoined a less strenuous retirement Lane turned his attention to the autopsy material collected by his friend the late Prof. F. W. O'Connor, of Columbia University, for the elucidation of the life-history of *Wuchereria bancrofti* in the human body and the puzzle of nocturnal periodicity. His last years were spent in careful and repeated methodical examination of these serial sections. Shortly before his death he finished his task. The results have not yet been published, but they offer further evidence in support of the view held by O'Connor and himself that the microfilariæ have a life-cycle of 24 hours.

"Clayton Lane was perhaps not easy to know," a friend adds, "for he did not suffer fools in any way, and about himself he was always tight shut as a clam. But those few to whom he gave his friendship found him a kindly, modest, staunch, and spiritually minded man." He died at his home at Ealing on Jan. 2 at the age of 80.

RICHARD CECIL HUTCHINSON

M.D. MANC., D.P.H.

Dr. R. C. Hutchinson, who died on Christmas morning at Worthing, where he had worked for 20 years, was a Lancashire man. In 1910 he graduated M.B. with honours at Manchester University, and after holding house-appointments at Manchester Royal Infirmary and the Brompton Hospital, London, he was appointed to the staff of the King Edward VII Welsh National Memorial Association, where he was in charge of the Carmarthen and Cardigan area. He returned from two years' service with the R.A.M.C. in France to become medical superintendent successively of the Baguley Sanatorium, Manchester, the Royal National Hospital, Ventnor, and the Tor-na-Dee Sanatorium, Banchory.

In 1928 Hutchinson moved to Worthing. Quiet and kindly in demeanour, a thoughtful and thorough clinician, he was at once a success in private practice. His long experience of chest work stood him in good stead, and his knowledge and skill in that branch of medicine were quickly recognised. It was not long before he was overworked, and he never spared himself. During the late war he gave fine service to the Royal Sussex County Hospital, working long hours in the outpatient department and then, in the winter months, driving home twelve miles in the black-out. He had also served the Brighton and Sussex Medico-Chirurgical Society as secretary, and, had he lived, would soon have been its president.

A keen sportsman and country-lover, "Hutch" was equally happy with rod or with gun. Those of us who spent holidays with him knew also his faithful companion "Bogie," whom he had trained with infinite patience, from a pup into a fine gun-dog. Last August, "Hutch" caught his last salmon from a boat and shot his last grouse from a butt, knowing that wading and walking-up had become beyond him. His family life was happy, and he is survived by his widow, two married daughters, and a son. Shortly before his death he had after a long search found a farm in West Sussex for his son, where he hoped to live and to continue his work at lessened pressure.

Many of his patients, friends, and colleagues attended the service held in his memory at Christ Church, Worthing, on Dec. 29.

D. H.

Diary of the Week

JAN. 16 TO 22

Monday, 17th

HUNTERIAN SOCIETY
8.30 P.M. (Mansion House, E.C.4.) Dr. John M. Finney, jun. (Baltimore): Founding and Influence of a School of Surgery. (Hunterian lecture.)

Tuesday, 18th

UNIVERSITY COLLEGE, LONDON
5.15 P.M. (Physiology Theatre, Gower Street, W.C.1.) Dr. E. Ashworth Underwood: Development of Modern Physiology, 1700–1900—Blood and Circulation. (First of 4 lectures.)

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. R. M. B. MacKenna: Principles and Practice of Treatment.

ROYAL PHOTOGRAPHIC SOCIETY, 16, Prince's Gate, S.W.7
7 P.M. *Medical group.* Dr. Peter Hansell: Observations on American Medical Photography.

Wednesday, 19th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
3.30 P.M. Mr. V. E. Negus: The Larynx.

HARVEIAN SOCIETY OF LONDON
8.15 P.M. (26, Portland Place, W.1.) Mr. E. G. Muir: A History of Surgery. (Presidential address.)

Thursday, 20th

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Dr. H. C. Trowell: Malignant Malnutrition (Kwashiorkor).

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, S.W.1
4.30 P.M. Psychiatry lecture-demonstration.

MIDDLESEX COUNTY MEDICAL SOCIETY
3 P.M. (Park Lane Health Centre, N.17.) Dr. G. Hamilton Hogben: Health Centre Experimentation. Mr. J. F. Pilbeam: New Developments in Public Dental Services. Dr. F. Carter: Aftercare as a Public-health Responsibility.

UNIVERSITY OF DURHAM
5 P.M. (Royal Victoria Infirmary, Newcastle-on-Tyne.) Sir Henry Dale, O.M.: Physiology and Surgery. (Rutherford Morison lecture.)

Friday, 21st

FACULTY OF RADIOLOGISTS
2.15 P.M. (Royal College of Surgeons, Lincoln's Inn Fields, W.C.2.) Dr. R. A. Kemp Harper: Radiological Investigation of Pancreatic Disease. Dr. A. E. Barclay, Prof. F. H. Bentley: Vascularisation of the Human Stomach and the Shunting Effect of Trauma.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY
7.15 P.M. (South Kensington Hotel, 41, Queen's Gate Terrace, S.W.7.) Prof. John McMichael: American Medicine.

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. N. S. Plummer: Pain in the Chest.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh
8 P.M. Sir Henry Dale: Medical Research as an Aim in Life.

Saturday, 22nd

BIOCHEMICAL SOCIETY
11 A.M. (Postgraduate Medical School of London, Ducane Road, W.12.) Short papers.

BRITISH ASSOCIATION OF ALLERGISTS (University College Hospital medical school, W.C.1)
11.30 A.M. Annual meeting.
2.15 P.M. Prof. C. Rimington: Biochemical Investigations of the Allergens of Household Dust.

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Notes and News

THE HOSPITAL AS GUEST HOUSE

ADDRESSING the London County Medical Society on Jan. 5, Mr. J. R. M. Whigham, the retiring president, said that the ideal hospital had yet to be built. Design must be related to function, and "job • efficiency" had always to be kept in mind; nowhere in the hospital was this more necessary than in the ward—the heart of the hospital and the very unit that somehow had been neglected. "We must have pity on the nurses' feet," he said, "especially in the performance of routine duties."

The last thing a patient wanted to do was to come into hospital, where he found himself in strange surroundings. To dispel this strangeness everyone coming into contact with the patient from the doctors downwards had to make the hospital what its name implied—a place for guests. A ward was in a sense a public place and certain self-imposed standards of behaviour were natural in all who lived and worked in it, but unfriendliness there need never be. Subdivided wards with opportunities for recreation for those able to enjoy it, were urgently needed.

For the doctor hospital medicine was not total medicine, and every opportunity should be taken to fill in the gaps, studying the patient in the light of his family, his house, his job, and his pay. Ideally every patient should have the best possible opinion at the earliest possible moment, and an attempt to achieve this ideal was made by delegating the work to juniors, not by reference in the reverse direction. Close contact with the relatives was desirable, and the transference back to the general practitioner of the patient should be accompanied by a full account of his case, not forgetting the prescription—"so important is it that the medicine is the same colour afterwards."

Doctors were not immediately concerned with the rising costs of hospital treatment; but by careful scrutiny they could make sure that the fullest use was made of beds in their charge. Some of the aged sick who were admitted should be at home, and no-one wanted this more than the patients themselves. Unhappily the patient sometimes had no-one to look after him at home; or the home, hardly fit to live in, was unfit to die in. No two hospitals were alike; each, having its own problems, must be allowed a measure of autonomy.

DELAYED NOBEL PRIZES

IN 1938 the Nobel prize for chemistry was awarded to Prof. Richard Kuhn, of Heidelberg, for his work on carotenoids and vitamins, and in 1939 it was divided between Prof. Adolph Butenandt, of Berlin, and Prof. Leopold Ruzicka, of Zurich. The *Times* reports that Professor Kuhn and Professor Butenandt are now to receive the prizes, which the Nazi government prevented their accepting.

The work of Professor Butenandt, who was then director of the Kaiser Wilhelm Institute for Biochemistry, has had important results for medicine. Having served an apprenticeship under Windaus, at Göttingen, he went to the chair of chemistry in the then free city of Danzig, and later to the Kaiser Wilhelm Institute, to fill the chair vacated by the removal of Neuberg. German workers had been quick to recognise the implications of the findings of Aschheim and Zondek, and Butenandt was supplied with large quantities of extract of the urine of pregnant mares for the isolation of the œstrus-producing hormone. Within a short time a series of brilliant papers began to come from his laboratory. The material was obtained in crystalline form by Butenandt at roughly the same time as a number of other investigators, and his brilliant degradation work demonstrated clearly the constitution of œstrone. He went on to make fundamental contributions on the constitution and partial synthesis of progesterone and the isolation and characterisation of androsterone. He visited this country several times before the war and lectured, in lucid English, in the University of London.

CHANGES IN POISONS LIST AND RULES

IN accordance with recommendations by the Poisons Board, the following changes are to be made in the law relating to poisons:

6-morpholino-4: 4-diphenylheptane-3-one ('Heptalgin') and its salts will be added to part I of the Poisons List.

Dinitrocresols will be taken out of part I and added to part II of the Poisons List.

Bis-bis-dimethylaminophosphorus anhydride, diethyl-*p*-anitrophenyl thiophosphate, hexaethyl tetrophosphate, and tetraethyl pyrophosphate will be added to part II of the Poisons List.

6-morpholino-4: 4-diphenylheptane-3-one will be included in the first and fourth schedules to the Poisons Rules.

Dinitrocresols will be exempt from the restrictions which apply to first and fourth schedule poisons when sold in the form of agricultural and horticultural insecticides or fungicides. Such preparations will be excluded from the general exemption from control of all substances containing dinitrocresols and not being preparations for the treatment of human ailments; they will be the only preparations containing dinitrocresols and subject to the control of the poisons law which may be sold by listed sellers of poisons.

The four phosphorus compounds already named will be exempted from control when sold in any form other than agricultural or horticultural insecticides or fungicides. These preparations, and the similar preparations containing dinitrocresols, will be subject only to the restrictions imposed by their being included in part II of the Poisons List and in the seventh schedule to the Poisons Rules: the form of words with which they are to be labelled will draw attention to the danger of using the preparation in an enclosed place and of allowing it to come into contact with the skin.

Registered veterinary practitioners will be given the same facilities for obtaining, supplying, and dispensing poisons as are enjoyed by registered veterinary surgeons.

Rule 18 will be amended to provide that a poison may be labelled with the approved name given it by the General Medical Council.

Rule 30 will be extended to include insulin in the list of poisons which may be manufactured under the supervision of a duly qualified medical practitioner.

Rule 31 will be amended to provide that the application to be listed as a seller of poisons shall be made in duplicate and that one copy shall be endorsed by the local authority and returned to the applicant.

University of London

At recent examinations for the M.D. degree the following were successful:

Branch I (*Medicine*).—Philip Arnold, Sivasithamparam Balasingam, F. A. Binks, V. M. Borrelli, W. F. Cavenagh, F. B. Charatan, A. G. C. Cox, R. H. Cutforth, J. J. Y. Dawson, Vincent Edmunds,* I. G. Fergusson, J. W. Gallant, Oliver Garrod, Irving Gilbert, Audrey Hanson, J. C. Harland, G. P. Hartigan, W. M. R. Henderson, Jack Henneman, J. W. Jordan (*B.Com.*), P. G. Keates, C. W. Kesson, H. A. Leggett, R. R. H. Lovell, K. M. Mackenzie, J. C. H. Maidment, T. P. Mann, R. M. Mayon-White, I. C. L. Patch, J. H. S. Pettit, T. R. E. Pilkington, Alexander Poteliakhoff, Frank Riley, R. W. Rowan, J. R. Sinton, H. E. Thomas, H. R. Thomson, M. H. West, J. B. Wild.

Branch II (*Pathology*).—J. A. H. Brown, M. G. H. Cooray,* R. H. Gorrill, N. F. C. Gowing, R. H. Heptinstall, Joseph Marks, R. D. de A. Seneviratne, D. A. Stanley, J. B. Walter, A. J. N. Warrack.

Branch III (*Psychological Medicine*).—T. G. Williams.

Branch IV (*Midwifery and Diseases of Women*).—Aileen M. Dickins.

Branch V (*Hygiene*).—J. B. M. Davies, R. E. Lane.

Branch VI (*Tropical Medicine*).—D. A. B. Hopkin.

* University medal.

On Thursday, Jan. 27, at 1.5 P.M. at University College, Prof. J. B. S. Haldane, F.R.S., will speak on Some Modern Views on Evolution.

On Thursday, Feb. 10, at Westminster Medical School, Horseferry Road, S.W.1, at 5 P.M., Sir Hugh Cairns will give a lecture on Surgical Aspects of Meningitis. At the same time and place on Feb. 24 Prof. R. G. Maegraith will discuss Malaria as a World Problem.

University of St. Andrews

At recent examinations the following were successful:

M.B., Ch.B.—H. M. G. Ewan, Jean A. Houston, Maria I. Insh, B. R. B. Lumb, A. H. Moyes, Phyllis Norrie, W. P. R. Rintoul, Averil J. Smith.

Social and Medical Legislation in the U.S.A.

President Truman's message on the state of the Union was delivered on Jan. 5 before a joint session of the House of the 81st Congress. In the course of his address he said: "The present coverage of the social-security laws is altogether inadequate and benefit payments are too low. One-third of our workers are not covered. Those who receive old-age and survivors insurance benefits receive an average payment of only 25 dollars a month. Many others who cannot work because they are physically disabled are left to the mercy of charity. We should expand our social-security programme, both as to size of benefits and extent of coverage, against economic hazards due to unemployment, old age, sickness, and disability. We must spare no effort to raise the general level of health in this country. In a nation as rich as ours, it is a shocking fact that tens of millions lack adequate medical care. We are short of doctors, hospitals, and nurses. We must remedy these shortages. Moreover, we need—and we must have without further delay—a system of pre-paid medical insurance which will enable every American to afford good medical care."

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Scientific Film Association

This association is holding the first of a monthly series of screenings of recent films for teachers of medicine on Thursday, Jan. 20, at 6 P.M. at 11, Chandos Street, London, W.1. The programme will deal with pædiatrics and will include the following films: *Your Children's Sleep, Progress Afoot, A Case of Sturge-Weber Syndrome, Infant Care, Know Your Baby.*

Dental Teachers' Pay

The British Dental Association is reported by the *Times* (Jan. 8) to have sent the following resolution, unanimously adopted by the council, to the Government Departments concerned:

That the council of the British Dental Association urges the Ministries of Health and Education to take such steps as will secure that the remuneration given to dental surgeons engaged in all branches of dental teaching shall be adequate to ensure the future satisfactory development of dental professional education.

In an accompanying letter Mr. H. Parker Buchanan, the dental secretary, says that unless speedy action is taken efficient teaching will become impossible.

W.H.O. in Eastern Mediterranean Area

Representatives and observers from 20 countries have been invited to attend a W.H.O. conference in Cairo on Feb. 7, when the establishment of a regional office for the Eastern Mediterranean area is to be discussed. On Jan. 1 a regional office for south-east Asia was opened in New Delhi, and a special office for European countries devastated during the war was established in Geneva. Other regional offices are planned for Africa, the Western Pacific, and the Americas.

Dr. J. D. Cottrell has been appointed adviser to the United Nations Relief for Palestine Refugees; he will advise voluntary agencies on the health aspects of their relief programmes. Dr. Cottrell has said that the health situation of the 700,000 or more refugees from Palestine is deteriorating rapidly. Typhoid fever, dysentery, and other intestinal diseases are widely prevalent; and the problem of malaria is urgent.

Order of St. John of Jerusalem

The King has sanctioned the following promotions in, and appointments to, this order:

As Knight.—C. E. C. Wilson, M.B.

As Associate Knight.—J. N. Mehta, M.D., M.R.C.P.

As Dame.—Margaret Ellen Douglass, M.D.

As Commanders.—Lieut.-General Neil Cantlie, C.B., M.C., M.B. Cornelius Thompson, M.B., Major E. S. B. Hamilton, M.C., F.R.C.S., Colonel C. P. Gaboury, O.B.E., M.D., C. A. Verco, M.B., Brigadier R. A. Hepple, C.B.E., M.C., M.B., Isabel Elmslie (Lady Hutton) C.B.E., M.D.

As Officers.—I. H. Beattie, L.M.S.S.A., Colonel Malcolm MacEwan, D.S.O., O.B.E., D.F.C., M.B., Lieut.-Colonel D. W. C. Gawne, M.D., F.R.C.S., R. I. Hyder, M.R.C.S., Major T. D. W. Fryer, M.B., G. A. Macdonald, M.B., J. T. Whitley, O.B.E., M.B., H. R. Mustard, M.D., Lieut.-Colonel H. F. Summons, M.B.E., M.B., Brigadier F. A. E. Crew, M.D., E. W. Lonsdale-White, M.B., Captain S. A. Nield-Faulkner, L.R.C.P.E., H. M. Ayres, M.R.C.S., Anthony Tabone, M.D., Lieut.-Colonel G. N. Morris, F.R.C.S., Major C. D. Donald, M.B., A. W. Azzopardi, M.D., Mrs. Dora E. Wheeler, M.B.

As Associate Officers.—Ganpatrao Shivjee Vazkar, L.M. & S., Rai Bahadur Captain Kananbehari Sen Roy, M.B.

Hospital Appeals

Authorities have been notified that the Minister of Health regards it as improper for hospitals in the National Health Service to appeal for funds. Boards and committees are thus required to cease the following practices if they have not already done so: advertisements, requests to individual subscribers, the placing of collecting-boxes in public places, requests to patients for donations and contributory schemes conducted by the hospitals themselves, radio appeals, flag-days, bazaars, fêtes, and the employment of hospital staff in collecting of voluntary funds. (Staff may give their own time to outside voluntary efforts—e.g., Alexandra Rose Day—but the use of uniformed nurses for this purpose should cease.) There is no objection to the acceptance by boards or committees of gifts of money made by independent bodies, by individuals, or by the groups of hospital supporters now being formed in many areas; and these independent bodies can, if they wish, make appeals for the benefit of hospitals. Boards or committees should not participate directly or indirectly in appealing for, or in collecting, funds for their hospitals; but they are urged to encourage voluntary service.

Appointments

BRAITHWAITE, J. V., M.R.C.S.: M.O., Passenger Transport Undertaking, Liverpool.
CASSON, F. R. C., M.B. Lond., D.P.M.: clinical assistant, department of psychological medicine, King's College Hospital, London.
COCHRANE, THOMAS, M.B., B.SC. Glasg.: physician, outpatient department for diseases of the skin, Glasgow Royal Infirmary.
CONDON, J. R., M.B. N.U.I., D.M.R.: radiotherapist i.c. Lincolnshire radiotherapy centre, Scunthorpe and District War Memorial Hospital.
ORR, I. M., O.B.E., M.D. Glasg., F.R.C.S.E.: general surgeon, Preston Royal Infirmary.
SILVER, P. S., M.R.C.S.: venereologist i.c. Bolton Clinic, Lancs.
TIZARD, J. P. M., M.A., B.M. Oxfd, M.R.C.P., D.C.H.: asst. director, pædiatric unit, St. Mary's Hospital, London.

The Hospital for Sick Children, Great Ormond Street, London:
FISHER, H. J. W., M.B. Lond., M.R.C.P., D.C.H.: house-physician.
LARG, MARY, M.R.C.S., D.OBST.R.C.O.G.: house-surgeon.
MEYER, R. B., M.B. Camb., M.R.C.P.: registrar, department of psychological medicine.
PHILPOTT, M. G., M.B. Lond, M.R.C.P., D.C.H.: house-physician.
WELLER, S. D. V., M.D. Lond., M.R.C.P., D.C.H.: medical registrar and pathologist.

Glasgow Royal Infirmary:
BROWN, ALEXANDER, M.D. Glasg., F.R.F.P.S., M.R.C.P.E.: physician, outpatient department.
MCGIRR, E. M., M.B., B.SC. Glasg., F.R.F.P.S., M.R.C.P.: asst. physician, outpatient department.

Lancashire County Council:
Asst. divisional M.O.s:
BEBBINGTON, FRANCES, M.B. Lpool, D.P.H.
BRIDGE, GEORGE, M.D Manc., D.OBST.R.C.O.G.
HAMILL, MARY, M.B. N.U.I., D.P.H.
WATSON, J. C., B.A., M.B. Dubl., D.P.H.

Births, Marriages, and Deaths

BIRTHS

BAMBER.—On Dec. 31, in Liverpool, the wife of Dr. Godfrey Bamber—a son.
BURSTEIN.—On Jan. 2, in Liverpool, the wife of Dr. N. Burstein—a daughter.
CLAYTON.—On Dec. 13, in London, the wife of Squadron-Leader G. Clayton, R.A.F.—a son.
EMBLETON.—On Jan. 3, at Lockton, Wokingham, the wife of Dr. J. A. Embleton—a son.
GEORGE.—On Jan. 3, at Maldon, Essex, the wife of Dr. Keith George—a son.
GILRUTH.—On Jan. 1, the wife of Dr. J. G. A. Gilruth—a daughter.
LUNT.—On Jan. 3, at Bretby Park, Burton-on-Trent, the wife of Mr. Randle Lunt, M.CH.ORTH.—a daughter.
MORGAN.—On Dec. 31, the wife of Mr. J. D. Morgan, F.R.C.S.—a son.
PETERKIN.—On Dec. 31, at Dawlish, S. Devon, the wife of Dr. D. B. Peterkin—a son.
POWELL.—On Jan. 3, at Liphook, Hants, the wife of Dr. Denis Powell—a daughter.
PRENTICE.—On Dec. 17, at Colchester, the wife of Dr. Ian Prentice, M.C.—a son and a daughter.
SIMMONS.—On Jan. 1, at Andover, the wife of Dr. A. B. Simmons—a son.
WRIGHT.—On Jan. 3, in Edinburgh, the wife of Dr. A. W. Wright—a daughter.

MARRIAGES

CROWELL—GUNDERSON.—On Dec. 24, in London, Patrick Lawrence Crowell to Eileen Marguerite Gunderson, M.B.
GELSTHORPE—WHIDBORNE.—On Jan. 4, in Khartoum, Alfred Morris Gelsthorpe, D.S.O., D.D., to Elfrida Whidborne, M.B.
LUCAS—CICERI.—On Jan. 4, at Newport, Mon., Nigel Oliver Lucas, L.M.S.S.A., to Joan Nina Ciceri.
MACKENZIE—PERKINS.—On Dec. 23, Ernest H. MacKenzie, M.R.C.S., to Lilian M. Perkins.
PURDIE—ROBERTS.—On Dec. 18, in London, Anthony W. Purdie, F.R.F.P.S., to Erica M. G. H. Roberts, M.B.

DEATHS

ADDISON.—On Jan. 5, at St. Mary's, Isles of Scilly, William Bragg Addison, B.A., M.B. Camb., aged 85.
FALKNER.—On Jan. 7, at Bournemouth, Berkeley Foote Falkner, L.R.C.P.I., aged 81.
GRAHAM.—On Jan. 2, Thomas Graham, M.C., M.B. Edin., aged 72.
HODGSON.—On Jan. 2, at Maghull, Albert Ernest Hodgson, M.D. Edin., D.P.H., aged 68.
HOLTHOUSE.—On Jan. 2, Edwin Hermus Holthouse, M.A., M.B. Camb., F.R.C.S., aged 93.
MACLAREN.—On Jan. 6, in London, James Alexander MacLaren, M.B. Edin., aged 89.
MESSER.—On Jan. 1, at Lemington-on-Tyne, Andrew William Messer, M.B., B.SC. Edin., aged 82.
RUSSELL-CARGILL.—On Jan. 7, in London, James Alexander Russell-Cargill, M.B. Edin.
SADLIER.—On Jan. 5, at Masterton, New Zealand, Horace William Sadlier, M.A., M.B. Camb.
SANDS.—On Jan. 6, at Gringley-on-the-Hill, Howard Sands, M.B. R.U.I., aged 83.

CORRIGENDUM.—In the New Year Honours the name of Dr. C. E. Etheridge should have appeared under the heading M.B.E.

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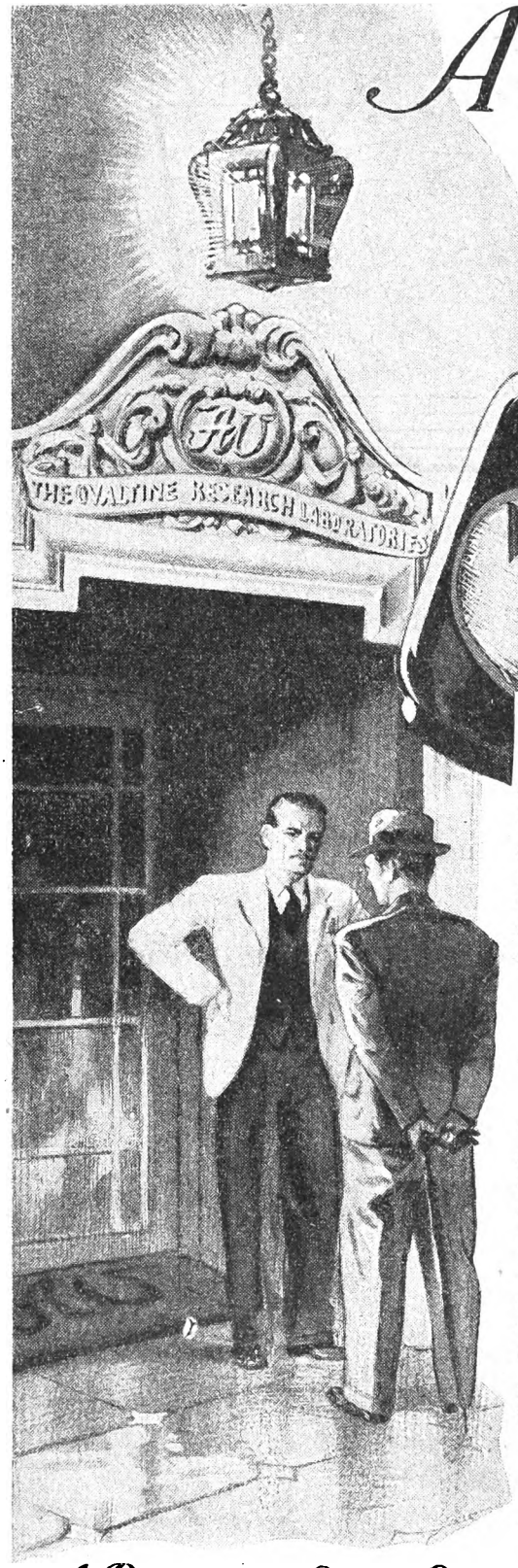

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MEDICINE IN THE NEW SOCIAL ORDER*

SIR FRANCIS FRASER
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DIRECTOR OF THE BRITISH POSTGRADUATE MEDICAL FEDERATION

THE community, be it represented by central government, local authority, professional association, or trade union, is now taking responsibility for many activities that were previously left to individual initiative. People are no longer as free as they were to decide the way they live and the contribution which each makes to the group or to the nation. They must submit to controls. The life of the individual has, of course, always been controlled, to an extent which has varied greatly at different times and in different places; but the extent of the control to which all in this country are now subjected is a new feature of the post-war years. This we can see already is producing changes in the personal relations of the individual to other individuals with whom he comes in contact, to the other members of his group, of his family, of his professional colleagues, of the team in which he works, and among his neighbours.

There have, of course, always been problems in human relations, individual and communal. It is the rate of change in the conditions of life today that make us so conscious of them. In the past, human relations and the personal difficulties and dilemmas to which they give rise have been solved with varying success, usually by the individual himself, often by members of the learned professions. Long before social sciences were thought of or the phrase human relations was accepted, the parson, the lawyer, and the doctor were practising an art for which we now seek scientific support. Today the universities are encouraging the development of the social sciences and giving a lead in their endeavour to train their graduates, the leading citizens of the future, to realise and tackle the difficulties. Surely then there is good reason for the learned professions, and medicine in particular, to consider their responsibilities and, if necessary, to amend their education to meet the calls which the community will make on their service.

In his *Short History of Medicine*, published in 1928, Dr. Charles Singer says:

> "When we glance at the tasks now performed by the medical man, we cannot fail to be struck by the great increase in the number of things that have come to be regarded as within his sphere. It is a commonplace that he has in large part taken the place of the parson. But he has also made encroachments on the functions of the lawyer, the legislator and the judge, of the schoolmaster, the architect, and the statistician. He has assumed some of the duties of the parent and guardian, while even the soldier and the policeman are to some extent under his control. In the ordering of their lives, and even in the regulation of their vices and the reform of their shortcomings, men and women are far more willing to seek the advice and help of the medical man than once they were. The reason is, without doubt, that his advice is much more worth having than ever it was."

In the exercise of his profession the medical man gains knowledge which he uses to good effect and so is able to advise and guide the people in the numerous ways recorded by Dr. Singer and many other ways besides. His professional education has not been designed to make him expert in these matters but it has had great value in the formation of character, the development of moral and cultural standards and ideals, and it is on the basis of these that he has come to occupy his place in modern society.

At the Congress of Universities of the Commonwealth held last July at Oxford, Prof. Boyce Gibson of Melbourne, discussing the social changes produced by the advances in science and technology, said:

> "The oldest of the technical studies, medicine, is intrinsically linked to the humane tradition; its purpose is the relief of suffering and the promotion of vital activity; success in its practice depends on the mastery of human personal relations; and its latest extension, psychiatry, requires, besides analytical competence, a compassionate insight into the human soul."

HEALTH IN THE NEW SOCIAL ORDER

We hear much nowadays of the right of everyone to a minimum standard of living, to food and housing, education, employment, care in old age and health. And by health is meant not merely treatment in sickness and the prevention of disease, but also the active promotion of health. In the *South African Medical Journal* of July 10 Prof. J. F. Brock, of Cape Town, distinguishes three factors affecting all diseases—inherited constitution, external agents (such as infection and trauma), and health-promoting factors. In the last group he puts food, exercise, sleep, warmth, air, cleanliness, education, and happiness. We have little exact knowledge of the influence on health of these latter—the intellectual and moral—factors, but evidence is steadily accumulating that the health of individuals is influenced by their happiness, even more perhaps than their happiness depends on their health.

This country can no longer afford to neglect any of its resources, and its greatest asset is the capacity of each member of the nation to contribute to the strength and efficiency of the whole, and this is governed largely by their health. Hence we may be sure that the advice of medical men will be sought in the coming years on many new matters affecting the health of communities and of individuals; and they should be well informed in order that their advice will be worth having. The list of things on which their help will be sought is almost inexhaustible, as it would include all aspects of life in a modern community. The most important factor of all, perhaps, and one on which advice is often needed, is the adjustment of human relations in order that any sense of injustice and frustration may be prevented or removed. In our complicated and controlled society this cause of unhappiness is becoming more frequent and its importance to health is coming to be appreciated more clearly as the natural history of disease is more widely studied.

THE CHALLENGE TO MEDICINE

There is evidence that the Government departments concerned with recent legislation and responsible for the numerous regulations and directions that have been issued for the administration of the new Acts are fully conscious that the people require guidance to enable them to adjust their lives to the new order. Large numbers of inspectors from the various ministries and departments, information bureaux, resettlement officers, health visitors, almoners, social workers, and so on, are being appointed to ease the difficulties of personal readjustment. Will they not suffice? Is there need for doctors also to concern themselves with these matters? I am confident that there is, for the responsibilities of each of these lay officials are highly specialised. Each will be expert in one aspect only of the life of an individual in relation to the community, one factor only in the health of the individual. But medicine has responsibility for the whole man—for his physical and his mental health, and for all the factors on which they depend.

The changes that are now taking place are the country's reaction to two world wars, to the exhaustion of its reserves, to the need for greater efficiency that it may retain its place among the nations. The medical profession is being challenged to play its part and make its peculiar contribution as the guardian of the people's

* From an address given to the Royal Medical Society in Edinburgh on Nov. 19, 1948.

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health. The challenge is above all to the family doctor and general practitioner.

The past shows that it is to him that families and individuals turn for help and advice, and to him they will continue to turn. Lay officials cannot take his place. His position in society is one of special privilege and trust. He represents the community when he helps us into the world and when he certifies that all is seemly when we die. He shares all the major crises of our lives. His knowledge of curative medicine gives him access to the private and personal affairs of the people; his education and his culture bring him forward as a leader in his community; compassion and human sympathy are inseparable from his calling; and ideals of service are passed on to him by his elders and by the traditions of his profession. The health of each member of the community will depend on his guidance, and all will look to him for help and advice, so that in adapting their lives to changing conditions they may not only safeguard their health but also improve it.

At present the general practitioner is having a bad time. He has so much to do that he is in danger of losing that joy in work well done which is essential to happiness. This is, I believe, a passing phase, and I hope that before long he will be relieved of much of the certification and paper work of all kinds which could be done as well by others, with the development of health centres and group practice, he should be relieved to an increasing extent of his present almost intolerable burdens. It might well appear impracticable now to suggest that his responsibilities in the new social order will be increased, but altered, I have no doubt, they will be. His training and his intimate knowledge of individuals and families point to him as the counsellor best qualified to help the individual to adjust his life.

EDUCATION OF THE DOCTOR TOMORROW

The undergraduate curriculum is concerned primarily with the broad principles of medical science on which efficient practice can be built as experience and wisdom are acquired. It would, I am sure, be a mistake at present to alter it to any great extent. But the post-graduate years offer better opportunities for education in the new duties and responsibilities of the medical profession. Under the National Health Service Acts the different branches of medicine—general practice, hospital practice, and the public services—will be more closely linked and postgraduate education will be encouraged. The universities have undertaken to develop postgraduate medical education, and it should thus be possible to keep doctors abreast of the progress of knowledge. It is highly desirable that the plans for different parts of the country should vary. Not only do conditions vary, but the experience gained from originality and initiative in one area may be of value to others.

There is likely, however, to be a general pattern of postgraduate education throughout the country in which the specialist clinical staffs of regional hospitals will be kept in constant touch with teaching hospitals and medical schools, and the general practitioners will be kept in touch with the specialists by means of clinical assistantships, regular meetings for discussion, and periodic refresher courses at the regional hospitals and the teaching centres. Through the specialist domiciliary service the family doctor will meet the specialists in consultation. It will be the responsibility of the specialist to keep up to date his own knowledge not only of diagnosis and treatment but also of the preventive and health-promoting factors that affect his specialty, and to understand how the provisions of public administration can be used for the benefit of his patients; and he will take every opportunity to pass on this information to the family doctor. To these ends he must watch the results of research in the social science, and seek to apply them to the practice of medicine. But there will be a two-way traffic, for the family doctor, aware as no-one else can be of the problems of individuals and their empirical solutions, will point out where new knowledge is needed. The family doctor should also be given opportunities for discussion with those responsible for the health of communities, the medical officer of health, the industrial medical officer, the school medical officer, and the medical administrator.

The scheme outlined in a recent circular of the Ministry of Health for the training of assistants by selected general practitioners is welcome. It should enable the older practitioners to hand on to the coming generation something of their wisdom and experience—something which the undergraduate curriculum cannot provide and which no form of organised postgraduate instruction can give—and to enable the general practitioner of the future to start his career, if not where his predecessor leaves off, at least somewhere well in advance of where his predecessor began.

THE DOCTOR'S PLACE

Close coöperation of general practitioners, specialists, and medical officers of public bodies and other organisations is necessary nowadays if the people are to have the full benefit of the knowledge now available. As the friend and counsellor of individuals and of families, the clinician, and especially the general practitioner, will be called upon not only to care for them in sickness, guide them in convalescence, advise them on the preservation of their health, but also help them to improve it. To these ends the medical man of the future must take an increasingly important place in the new social order, helping each individual to adjust his life successfully to the rapidly changing conditions, for in this way only can the people be happy and healthy, and contribute in full measure to the well-being of the society to which they belong.

DEXTRAN AS A PLASMA SUBSTITUTE *

GUNNAR THORSÉN
M.D. Stockholm
SURGEON TO OUTPATIENTS AND ASSISTANT PROFESSOR OF SURGERY, SERAFIMER, STOCKHOLM

IN 1943 Grönwall and Ingelman, in Sweden, suggested the use of dextran as a substitute for plasma. This colloid is free from the drawbacks of other colloids previously prepared as substitutes for plasma.

Clinical trials were made at the Central Hospital, Örebro, and later at the Serafimer Hospital, Stockholm, and after various tests and modifications the dextran now in use was produced. Brief reports of the results of subsequent clinical trials have been published by Grönwall and Ingelman (1944a and b, 1945a and b),

* From a paper read to the annual meeting of the Association of Surgeons of Great Britain and Ireland on May 6, 1948, in Edinburgh.

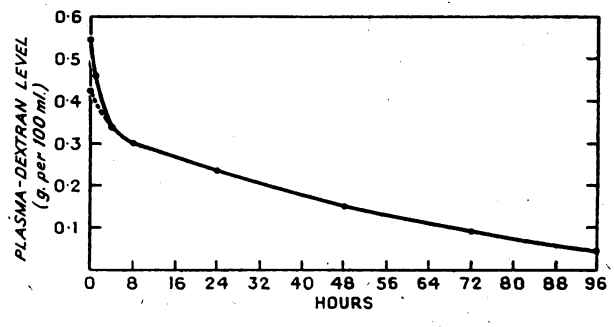

Fig. 1—Plasma-dextran level after infusion of 400 ml. of dextran Ph.

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Bohmansson et al. (1946), and myself (Hint and Thorsén 1947, Thorsén 1948). In 1945 samples of Swedish dextran, produced on a semi-commercial basis, were sent to the Lister Institute. In 1946 samples of dried dextran were sent to prominent scientists in the United States for the preparation of solutions and testing.

The dextran now in use is 'Dextran Ph,' a proprietary preparation produced by the Swedish firm Pharmacia. It is a 6% solution of the polydispersoid glycose-polymer dextran, in which most of the molecules have been hydrolytically given a molecular weight conforming to that of albumin, with 0·9% of sodium chloride added to it. Its viscosity lies between that of blood and that of plasma, and its specific gravity somewhat exceeds that of human plasma. Dextran is virus-free, does not lead to the formation of antigens, and contains almost no nitrogen. Its thread-like molecules are electrically neutral and chemically indifferent.

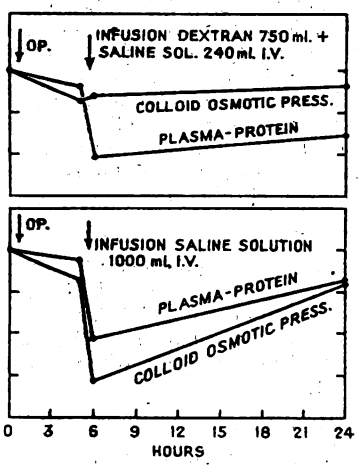

Fig. 2—Colloid osmotic pressure and plasma-protein levels after infusion of dextran Ph and physiological saline solution (above) and of saline solution alone (below).

Dextran has been given to 5000 patients, 20,000 units having been infused. In a few cases up to 4 litres has been given in a single infusion. The largest amount given to any one patient has been 10 litres. Dextran is non-toxic and does not injure the tissues either locally or systemically. The results obtained with it have been very good both in the treatment and in the prevention of shock. At the hospital dextran is used as a routine in the prevention of shock during major operations. A series of controls in which corresponding amounts of physiological saline solution were given had a higher incidence of postoperative complications. Rosenqvist (1947) reported dextran to be as good as plasma in shock from burns. In Sweden today the hospital transfusion services rely to a large extent on dextran for emergency cases. Its use has not been found to affect fertility, fœtal development, or growth.

PLASMA-DEXTRAN LEVELS AND EXCRETION

After an intravenous injection of 1–2 litres of dextran the plasma-dextran level rises to 1–2·5 g. per 100 ml. Next, after an initial fall due principally to elimination of a low-molecular fraction through the kidneys, the plasma-dextran level falls at an even rate (fig. 1).

During the initial renal excretions of low-molecular dextran the urine-dextran level may rise to 7 g. per 100 ml. without any sign of renal injury. During this time about a quarter of the dextran given is excreted, provided an ordinary amount has been infused. After that no dextran can be detected in the urine by polarimetry, even though the plasma-dextran level remains relatively high. The mean molecular weight in the dextran excreted in the urine has been calculated at 25,000. Dextran of a higher molecular weight is presumably metabolised.

After the initial fall the plasma-dextran level falls at an even rate, which is more rapid in small animals than in large ones; the rate increases with the simultaneous administration of thyroid hormone; and is also related to the amount of dextran given.

The elimination of dextran not excreted in the urine takes place at a rate that differs slightly in different species of animal, as calculated per kg. of body-weight

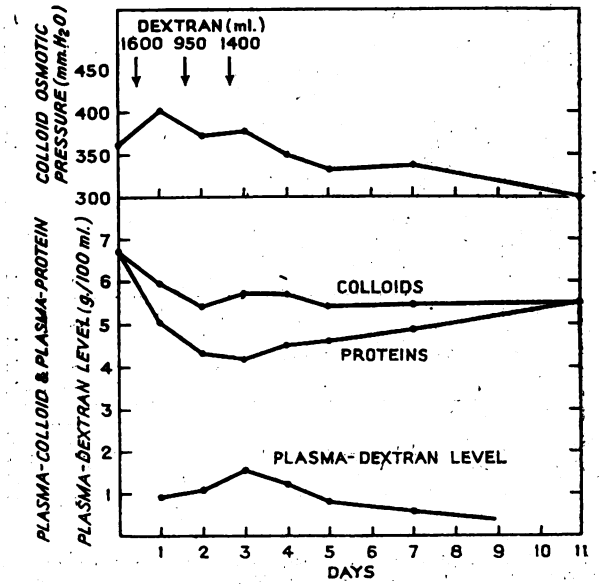

Fig. 3—Colloid osmotic pressure and plasma-colloid levels in peritonitis after intravenous infusions of dextran Ph.

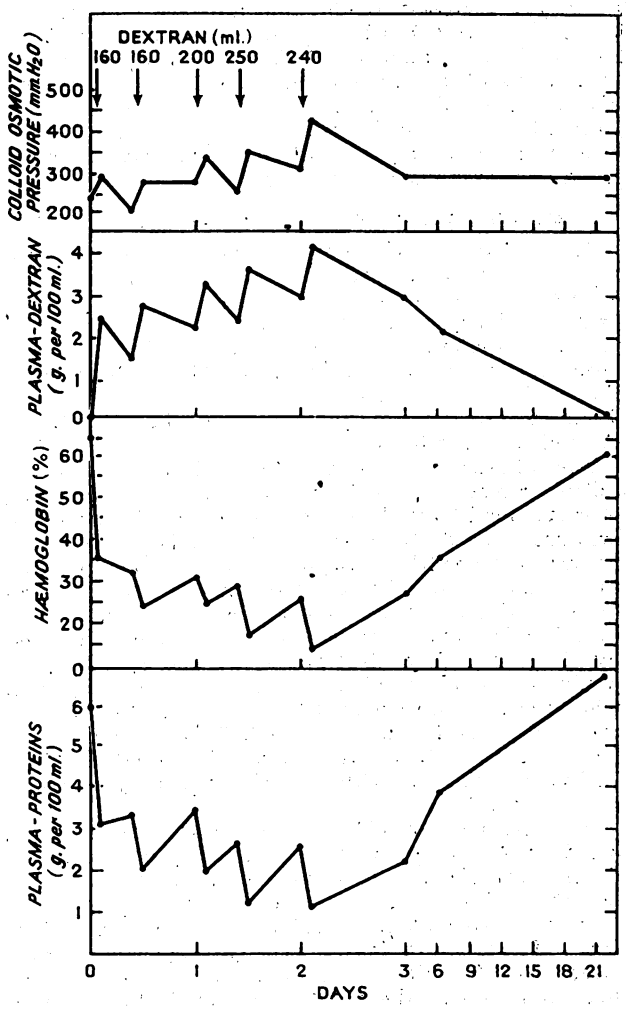

Fig. 4—Colloid osmotic pressure and plasma-protein levels in a rabbit weighing 3·55 kg. given repeated large infusions of dextran Ph.

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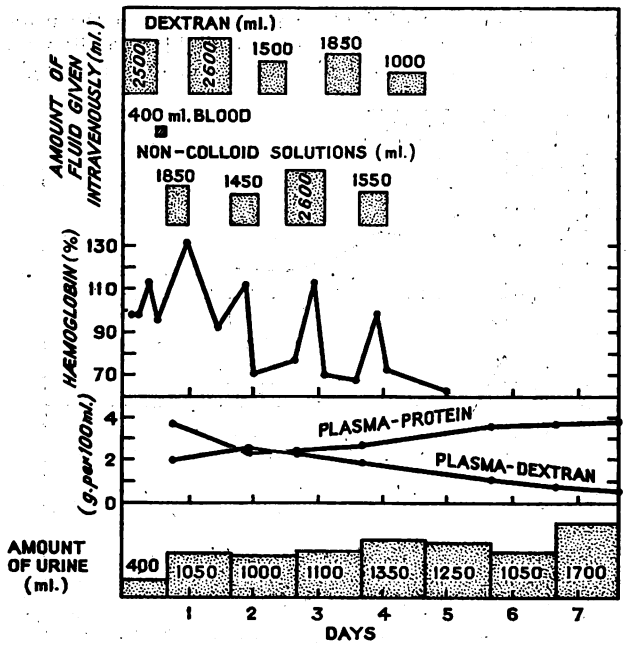

Fig. 5—Plasma-dextran and plasma-protein levels in shock due to burns (40% of body surface), showing haemoconcentration when non-colloid infusions are substituted for dextran Ph during protracted shock.

per day, irrespective of the amount given. In animals to which dextran has been given in repeated infusions, so that the total amount of dried substance corresponds to a third of the body-weight, no dextran has been discovered in the brain, lungs, heart muscle, liver, spleen, kidney, or bone-marrow, either by morphological changes or in watery extracts from the organs after it has disappeared from the plasma.

MAINTENANCE OF COLLOID OSMOTIC PRESSURE

The maintenance of a normal colloid osmotic pressure plays an important part in metabolism. This pressure affects the passage of fluid from the capillaries into the extravascular space, as well as its subsequent reabsorption into the capillaries. If the colloid osmotic pressure is lowered, the efflux of fluid increases, while simultaneously the reabsorption decreases. The resulting œdema diminishes the exchange of substances and gases between the cells and the blood.

The infusion of a non-colloid solution lowers the colloid osmotic pressure more than it reduces the plasma-colloid level. The lowering of the colloid osmotic pressure often deleteriously affects cellular metabolism, because the conditions requiring an infusion are often those associated with capillary injuries, and consequently with disturbed colloid osmotic pressure. This reduction in pressure can be counteracted and neutralised by giving parenteral dextran (figs. 2 and 3). This has produced notable results, especially in paralytic ileus, when the reabsorption of œdema fluid in the intestinal wall, following the increased colloid osmotic pressure, has manifested itself by restored intestinal motility. In hypoproteinæmia with œdema the urinary excretion is increased.

The normal colloid osmotic pressure, however, can be raised only slightly. If additional amounts of dextran are given only temporary increases in pressure are obtained (fig. 4), and the plasma-dextran level can be raised above 3·5 g. per 100 ml. for only a very short time. The excess of dextran rapidly disappears from the circulation. The plasma-dextran level after such amounts decreases slowly, the time taken for it to disappear corresponding to the quantity given. But the rate of elimination, expressed in g. per kg. of body-weight per day, is the same, irrespective of the initial amount infused.

Flooding of the extravascular space with dextran has not given rise to definitely unfavourable effects in the test animals, but it produces œdema. Such large amounts of dextran are not used clinically.

A raised plasma-dextran level is always associated with a lowered plasma-protein level. When later the plasma-dextran level falls, the plasma-protein level rises again (figs. 4 and 5).

No unfavourable effect from the simultaneous fall in the plasma-protein level has been noted clinically, even though the plasma-protein level has fallen to 2 g. per 100 ml. No sign of disturbed coagulation or reduction in the resistance to infection, in the formation of antibodies after the injection of tetanus and diphtheria anatoxin (Heinertz and Thorsén unpublished), or in the tensile strength of operation wounds has yet been noted either clinically or experimentally after the administration of dextran in therapeutic doses.

The factors, principally dilution and colloid osmotic pressure, acting as mentioned above as well as on the reciprocal concentration of the different fractions of plasma-proteins, have been investigated by Thorsén and Malmros (unpublished).

SUMMARY

Dextran Ph is a polydispersoid polymer of glycose with a molecular weight conforming to that of albumin. It is totally eliminated from the body and is non-toxic. It is very useful as a substitute for blood and plasma in cases where an increase in blood volume or in colloid osmotic pressure is desired.

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DEXTRAN AS A PLASMA SUBSTITUTE

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EXPERIENCE in the 1914–18 war showed that restoration of the circulating blood volume was the most effective single restorative measure in patients who had suffered severe injuries. Bayliss (1919) showed that a fluid which contained colloids having an osmotic pressure similar to that of plasma-proteins could be used as a substitute for blood. He tried soluble starch, dextrin, and gelatin, but discarded them as unsatisfactory. However, gum arabic had most of the desired properties, and a 6% solution in 0·9% sodium chloride was introduced for general use.

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Infusion of this "gum-saline" gave remarkably satisfactory results even in patients who had lost much blood. Evidently this was accomplished by increasing the venous return and thus increasing the cardiac output so that the available hæmoglobin, though reduced in amount, could be fully utilised. Gum-saline, by being retained in the circulation for long periods, maintains the blood volume at a satisfactory level until the patient can resynthesise his plasma-proteins. Various workers have since criticised gum-saline, mainly on the ground that the gum is stored in various organs, particularly the liver (Andersch and Gibson 1934, Dick et al. 1935), and that it interferes with liver function (Hall 1938). Other possible colloids for infusion, such as pectin, polyvinyl alcohol, and methyl cellulose, also show storage phenomena, and apparently lead to atheroma of arteries (Hueper 1942a and b).

During the 1939–45 war another synthetic colloid, polyvinyl pyrrolidone, was extensively used in Germany for intravenous infusion (Hecht and Weese 1943). It seems unlikely that the molecules of the vinyl polymers large enough to be retained by the glomeruli can be metabolised by the body; some form of storage may therefore take place.

Swedish workers, after very extensive clinical trials, have reported favourably on dextran solutions prepared in Sweden (Grönwall and Ingelman 1944, 1945a, Bohmansson et al. 1946, Rosenqvist 1947). Dextran has certain theoretical advantages over other non-protein colloids in that (1) it is free from acidic radicals, and therefore not likely to form storage complexes, and (2) it can be hydrolysed into glucose by acids and by certain living organisms which suggests that the human body may also be able to metabolise it slowly.

During the 1939–45 war human plasma and serum were prepared in large amounts; and as they are now widely available it might seem superfluous to pursue the search for a really satisfactory substitute for plasma. However, plasma and serum carry a definite though small risk of infecting the recipient with hepatitis or some other transmissible disease. Moreover there are climatic and geographical circumstances in which a stable plasma substitute which could be manufactured in unlimited amounts might be very valuable. Even where blood and plasma are readily obtainable, and even if it should prove possible to free plasma from all infective agents, it might still be an advantage to have reserves of a plasma substitute for use in some civil or military emergency. The main function of the substitute would clearly be to restore circulating blood volume until the patient's own plasma-protein returned to the circulation. Such a substance would suffer from the theoretical disadvantages of being unable to fulfil the nutritive, buffering, or immunological functions of plasma-protein; but, since usually it would only be taking the place of plasma-protein for a matter of hours, this could not be considered an important objection. It is also clear that a plasma substitute can never be more than second best when the patient has lost whole blood rather than plasma, and that infusion of a plasma substitute in such cases would have to be followed by transfusion of whole blood to secure the best clinical response.

REQUIREMENTS OF A PLASMA SUBSTITUTE

The theoretical requirements are as follows:

Positive Qualities

(1) Its colloid solutes should be retained in the circulation until their place can be taken by the natural proteins. This implies that (*a*) the colloids should not pass readily into the tissue fluids nor be rapidly excreted by the kidney (a molecular size of at least 70,000 is therefore usually desirable); and (*b*) the colloid substance should not be rapidly metabolised or otherwise removed by the tissues.

(2) The solution used for infusion should have an osmotic pressure and viscosity similar to those of plasma.

(3) The composition from batch to batch should be constant, within narrow and definable limits.

(4) The material should be stable during storage and preferably not require special conditions of temperature.

Negative Qualities

(5) It must not be toxic, either locally or generally.

(6) It must not induce fever.

(7) It must not induce sensitisation.

(8) It must not be stored for long periods in the tissues.

(9) It must not act as a diuretic. Apart from the absence of specific diuretic properties, this implies that it should not contain large amounts of solutes of low molecular weight.

All these requirements could be met by a solution of non-toxic non-protein material of suitable molecular weight which was slowly metabolised by the tissues. For maximum osmotic effect with the minimum of material, while still satisfying criterion 1*a*, the range of molecular size should approximate to that of plasma-albumin. The present study shows that dextran preparations can fulfil most of these requirements.

In 1946 the Swedish firm Pharmacia A.B. generously supplied some of their dextran, and it was possible to give this to a few patients and confirm that it was a bland fluid which produced favourable clinical results. Shortly afterwards dextran manufactured experimentally in Britain[1] became available, and it was possible to begin a more extensive trial.

CHEMISTRY OF DEXTRAN AS PREPARED FOR INFUSION[2]

Composition and Preparation

Dextrans are produced by the growth in culture of various micro-organisms, in particular of the non-pathogenic coccus, *Leuconostoc mesenteroides*, in a substrate of sucrose and phosphate. The micro-organism produces an enzyme or enzymes which synthesise dextran from sucrose. After removal of protein and inorganic salts from the culture fluid, dextran is precipitated in the form of a syrupy gum by organic solvents such as acetone; so obtained, it is a polysaccharide composed entirely of glucose units. Each unit is joined by an alpha-glucosidic linkage to the primary alcoholic hydroxyl group of its neighbour. The long chains thus constituted may have occasional branch linkages to adjacent chains through other secondary hydroxyl groups. As with many other polysaccharides, the details and degree of this branching are uncertain.

Swedish workers tested this material for infusion but soon found that the molecules of crude dextran were too large for this purpose. More encouraging results were obtained with preparations whose average molecular size had been reduced by partial hydrolysis with acid (Grönwall and Ingelman 1945a and b, Bohmansson et al. 1946). To avoid confusion in the following paragraphs we use the term "undegraded dextran" for the polysaccharide synthesised from sucrose, and "dextran" for the degraded product produced by acid hydrolysis.

The British company which began dextran production in this country has developed a process for freeing the product from protein and for controlling the range of molecular sizes. Two batches of their material were supplied for trial. The solutions were colourless or of

1. Prof. Sir Norman Haworth and Prof. M. Stacey, of the department of chemistry, University of Birmingham, had been interested for some years in the chemistry of dextran and in the idea of using derivatives of dextran and other polysaccharides as blood-plasma substitutes. Following the Swedish publications, work was continued independently at Birmingham, and samples of degraded dextran were made available for experimental trial. In this work Mr. G. Swift, Ph.D., and Mr. A. R. Lockwood were intimately concerned, and it was largely as a result of the work of this team that experimental batches of dextran became available in this country for clinical trial.
2. The physicochemical and biochemical measurements in this and subsequent sections were made by C. R.

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a pale straw colour, and of about the same specific gravity and saline concentration as plasma. Details are as follows:

	GL/50/2	GL/50/3
Batch no.		
Dextran (g. per 100 ml.)	6·35	6·29
Sodium chloride (g. per 100 ml.)	0·86	0·94
Nitrogen (mg. per 100 ml.)	< 1·0	<1·0
Relative viscosity [3]	5·4	4·1
Specific gravity	1·026	1·025
pH	7·0	6·9

These solutions had a colloid osmotic pressure 1·5–2·0 times that of normal plasma.

Outline of Methods of Estimation

For satisfactory assessment of its value for resuscitation, methods of estimating dextran in infusion solutions, blood, tissue fluids, and tissue extracts are required. There are two principles upon which such estimation can be based. The more fundamental is the hydrolysis of the dextran and the measurement of the resulting glucose. This method has accordingly been developed, and the conditions have been worked out for the full hydrolysis of dextran by acid so that decomposition of glucose is avoided. Then the glucose is estimated by the method of Schaffer and Hartman (1921).

The method of Hint and Thorsén (1947) uses a different principle, depending on the formation of a complex between dextran and copper which is insoluble in alkaline solution. Under these conditions copper is removed quantitatively by the dextran. After the amount of copper remaining has been determined colorimetrically with diethyl-dithiocarbamate, the amount of dextran can be calculated from a calibration curve. Alternatively the copper-dextran complex can be isolated and the colour given with indole and sulphuric acid used for estimation of the dextran (Goldenberg et al. 1947). In the clinical trial the hydrolytic method was used for estimating dextran in the bottles supplied by the manufacturers and in urine samples. The unmodified copper-complex method of Hint and Thorsén was used for plasma samples, after a calibration curve had been prepared by mixing dextran solutions of known composition with plasma. A slight modification of the copper-complex method enabled it to be used for urine samples as well.

Methods of Delimiting Molecular Size

The partially hydrolysed dextran used for infusion contains molecules of different sizes. As stated above, its efficiency depends on the range of sizes of molecules and the mean molecular weight. Several physicochemical methods help to define these quantities.

In general, *osmotic pressure* depends on the relative concentrations on the two sides of a semipermeable membrane. As well as being of direct importance in an infusion fluid the osmotic pressure is thus also a measure of the mean molecular size of substances to which the membrane is impermeable. When dextran solutions are put up in osmometers, such as are used for plasma-proteins, there is difficulty in establishing equilibrium. The small molecules of dextran pass through the membranes, which are impermeable to hæmoglobin, and the initial pressure reading is not maintained. Dextran can then be detected outside the semipermeable sac. When about 85% of the dextran was first separated by acetone precipitation and then redissolved, this solution of the larger molecules came to a satisfactory equilibrium in the osmometer. The results indicate a mean molecular size of 75,000 ± 10% for this fraction.

The *viscosity* of a solution is a further guide to the molecular size of the colloids it contains. In general, the higher the viscosity the larger the molecules, but with mixtures of colloids of different sizes viscosity is liable to be unduly affected by large molecules. It thus yields reliable results only when the distribution of molecular sizes around the mean is similar in the solutions compared. This principle has been used to compare the mean molecular sizes of different batches of dextran.

Dextran excreted in the urine of a patient transfused with batch GL/50/2 was shown by viscosity measurements to have a much lower molecular weight than that of the material infused. This finding is in line with the demonstration by osmometry of the presence of small molecules in a dextran solution. The early excretion of about a fifth of the material appears to be a filtering off of this small molecular fraction.

Another procedure which depends on the molecular size of dextran is its *fractional precipitation* by acetone. When acetone is added to a dextran solution the larger molecules precipitate first; but, as more is added, progressively smaller molecules come down. This method does not give a precise division at a particular molecular size, but it provides a practical test of the approximate limit to the range of sizes present in a solution.

On the basis of these studies it is possible to determine closely the composition of a preparation of dextran. For example, in batches GL/50/2 and GL/50/3 the range of molecular size was such that no dextran could be precipitated by the addition of 42 ml. of acetone to 100 ml. of the solution, whereas the addition of 122 ml. of acetone caused complete precipitation.

EXPERIMENTAL OBSERVATIONS [4]

The batches of British dextran used in this pilot trial have been examined in the laboratory to exclude toxicity, pyrogenicity, and antigenicity; to investigate their effectiveness in restoring the blood-pressure of animals which have been bled; and to ascertain the fate of dextran in the body after injection.

Toxicity

Dextran has been injected intravenously in volumes up to 1 ml. in mice without producing any harmful effects. Likewise, rabbits receiving injections of volumes from 10 ml. per kg. of body-weight per day for four days to 22 ml. per kg. per day for seven days have shown no abnormal clinical signs during, or for periods up to fourteen weeks following, the course of injections. Albuminuria and hæmaturia have not been observed.

In guineapigs no significant difference has been detected in the cutaneous reactions following the intradermal injection of saline solution and dextran.

3. The relative viscosity is obtained by dividing the flow time for dextran in an Ostwald viscometer by the time for water in the same instrument. Measurements were made at 37°C.

4. All the experimental observations, save those on pyrogenicity, were made by W. d'A. M. and S. J. L. S.

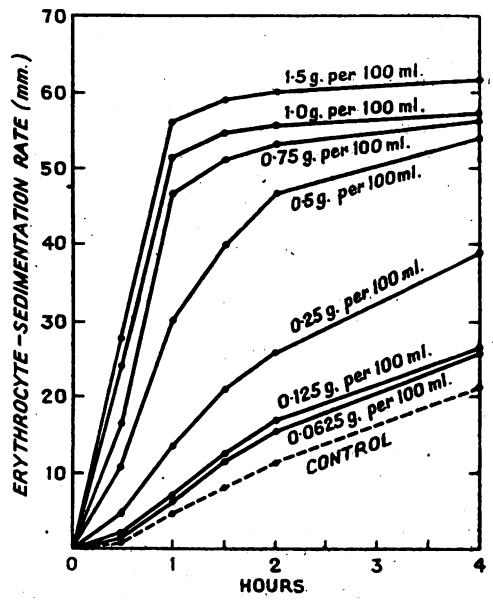
ERYTHROCYTE-SEDIMENTATION RATE (mm.)
HOURS
1·5 g. per 100 ml.
1·0 g. per 100 ml.
0·75 g. per 100 ml.
0·5 g. per 100 ml.
0·25 g. per 100 ml.
0·125 g. per 100 ml.
0·0625 g. per 100 ml.
CONTROL

Fig. 1—Effects of different plasma-dextran levels on erythrocyte-sedimentation rate (Wintrobe) in man.

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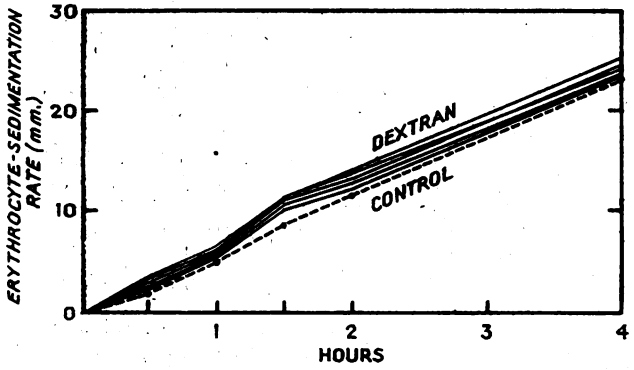

Fig. 2—Effects of different plasma-dextran levels (1·0, 0·5, 0·25, 0·125, and 0·0625 g. per 100 ml.) of dextran of molecular weight about 26,000 on erythrocyte-sedimentation rate (Wintrobe) in man.

The histological examination, at intervals of up to ninety days, of the liver, kidneys, spleen, cardiac muscle, thyroid, and suprarenal glands from rabbits used in the laboratory investigations has revealed no abnormalities.

Pyrogenicity

Through the kindness of Mr. F. C. McIntosh, PH.D. of the National Institute for Medical Research, Hampstead, all the batches have been subjected to the standard rabbit pyrogen tests in use in that laboratory. None of the batches of dextran, given in doses of 20 ml. per kg. of body-weight to groups of three rabbits, has been found to be pyrogenic. The maximal permissible rise of temperature in each rabbit was 0·6°C.

Antigenicity

No anaphylactic phenomena have been observed in guineapigs in which the induction of sensitivity was attempted by the intraperitoneal injection of 1 ml. of dextran. The gut and uterus were examined fourteen and twenty-one days later by the usual techniques.

The serum of rabbits injected with dextran intravenously (six doses of 0·6 ml. at two-day intervals) and bled eleven to fourteen days after the last injection has contained no antibodies demonstrable by the ring and precipitin tests. Nor have antibodies been detected in the sera, examined at various intervals after injection, of animals surviving substitution of half their blood volume with dextran or given courses of injections of dextran without preliminary reduction of the blood volume.

Restoration of Blood-pressure

In rabbits anæsthetised with pentobarbitone sodium, and rapidly deprived of about half their estimated blood volume by bleeding from a cannula inserted into one of the carotid arteries, the intravenous infusion of an equivalent amount of dextran restored the blood-pressure rapidly and maintained it for 3–3½ hours. The restoration of blood-pressure was more rapid than after transfusion with whole blood or infusion with saline solution; hence the infusions had to be given more slowly than with blood or with saline solution. The level to which the blood-pressure was restored was somewhat higher than after transfusion with blood or infusion with saline solution.

Erythrocyte-sedimentation Rate, Rouleaux Formation, and Hæmagglutination

Immediately after infusion the erythrocyte-sedimentation rate (E.S.R.) is increased and rouleaux can be observed in smears of blood. The alteration in the E.S.R. varies with the plasma-dextran level (fig. 1). Rouleaux have been observed when the plasma-dextran level is 0·5 g. or more per 100 ml., but not with levels of 0·25, 0·125, or 0·0625 g. per 100 ml. No increase in the osmotic fragility of the red cells has been observed after the transfusion of dextran.

Erythrocytes which have been exposed to dextran can readily be freed from it by washing, so that their reactions with grouping sera can be correctly determined. However, the presence of dextran in a patient's plasma may interfere with direct matching tests, by causing heavy rouleaux formation of the prospective donor's erythrocytes. This rouleaux formation may not be completely abolished by dilution of the plasma with an equal volume of saline solution, but on further dilution the rouleaux will disappear. Dilution of the patient's plasma with, say, three times the volume of saline solution before direct matching clearly cannot be recommended as a routine, because it might cause true but very weak agglutination to be overlooked; and, more important, might lead to overlooking the presence of a blocking antibody. However, in these circumstances direct matching by the indirect Coombs method would reveal the presence of incompatible blocking antibody. It is clearly best to obtain a sample of serum from the patient as a routine before giving an infusion of dextran, so that, if the patient later requires a blood-transfusion, serum free from dextran is available for a direct matching test.

In an attempt to discover whether the increased E.S.R. is brought about by large or small molecules of dextran, measurements have been made with degraded dextran of a molecular weight (about 26,000) considerably lower than that of the batches supplied for clinical trial (fig. 2). It will be seen that the E.S.R. varies little from the control over a range of plasma-dextran levels from 1·5 to 0·0625 g. per 100 ml. Similarly, rouleaux formation has been studied in a 5% suspension of red blood-cells in various concentrations of dextran in 0·9% saline solution as follows:

Dextran %	*Approximate Molecular Weight* 26,000	44,000	74,000	88,000
1·0	—	+	+ + +	+ + + +
0·75	—	+	+ +	+ +
0·50	—	—	+	+
0·25	—	—	—	+
0·125	—	—	—	—
0·0625	—	—	—	—
0·03125	—	—	—	—
0·0	—	—	—	—

\+ Few rouleaux of 4–8 cells.
\+ + Many short rouleaux.
\+ + + Many short and some long rouleaux.
\+ + + + Many short and long rouleaux; few free cells.

Though it has been impossible to determine the E.S.R. at other known higher molecular weight ranges, we may conclude that the larger molecules of degraded dextran are responsible for the increased E.S.R. observed after the infusion of dextran.

Fate of Dextran

As a means of detecting the presence of dextran in the tissues use has been made of the fact that antisera to *L. mesenteroides* precipitate with dextran (Evans et al. 1941, Sugg and Hehre 1942), which behaves as a haptene. It has been found that good antisera, prepared in rabbits, react with the dextran used in this trial in concentrations of 1 : 1,000,000 (sensitivity of the chemical method of Hint and Thorsén (1947), in our hands, 1 : 2000). The serological method of detecting dextran has been used in these experiments only as a qualitative test. Its use for the quantitative determination of dextran is being investigated, and will depend to some extent on the constancy of the molecular composition of the degraded polysaccharide.

The tissues of rabbits, which had been given dextran intravenously over seven days in amounts equivalent to 9 g. per kg. of body-weight (comparable with an infusion of 1·5 litres per day for seven days in the average adult),

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were perfused with physiological saline solution to remove blood; they were then minced, ground in sand, and extracted with a volume in millilitres of 0·9% saline solution roughly equivalent to the weight of the tissue in grammes. The resulting extracts were defatted by freezing with excess ether three times, separated, and centrifuged. The results obtained by the chemical and serological methods are shown in table I.

The tissues of uninjected rabbits, examined in the same way, have given negative results with both the chemical and the serological methods. The tissues of animals kept longer than eight weeks after receiving dextran are being examined.

Dextran was detected serologically in the urine of these rabbits, usually until the fifth or sixth day after the course of injections; in one animal it was detectable until the twelfth day.

No significant increase in urine volume was observed after the injection of dextran in volumes equivalent to half the blood volume. Comparable estimations on tissues of human patients are being undertaken.

Incubation of Dextran with Blood, Tissue Extracts, and Tissue Suspensions

Blood was mixed with a third of its volume of 6% dextran solution and the mixture was kept at 37°C for seven days. The fall in dextran concentration averaged 1·5% per 24-hour period, compared with 30–33% in the blood-stream of a patient. When dextran was incubated with saline extracts of guineapig pancreas and liver or with suspensions of finely ground rabbit lymph-gland, spleen, and liver, negligible changes in dextran concentration were recorded during 120 hours.

CLINICAL TRIALS

The preliminary trials, and the trials on patients undergoing major operations, were made at the Blood Transfusion Research Unit and in the departments of medicine and surgery at the Postgraduate Medical School of London, and the trials on patients with burns at the burns unit of the Birmingham Accident Hospital.

Preliminary Trials

It was decided that the initial infusions of British dextran should be given to patients with inoperable carcinoma; 6 such patients received an infusion of 300–500 ml. of dextran over periods of 30–90 min. No ill effects of any kind were noted. Temperatures were recorded half-hourly throughout each infusion and for three hours thereafter. In 5 of the 6 patients the temperature never rose above 98·4°F, and in the 6th patient, who had previously shown a small daily fever, the temperature rose to 99°F. No patient had local pain at the site of injection, and in no case was there any evidence of thrombophlebitis.

On the other hand, it was readily noted in this pilot trial that the infusion of dextran produced a rise in jugular venous pressure; and in 2 patients it was considered advisable to discontinue the infusions after 300 ml. and 400 ml. had been given, when it appeared that there was some risk of overloading the patient's circulation.

From this preliminary trial it was concluded that British dextran was bland, pyrogen-free, and well tolerated by the recipients.

Patients Undergoing Major Operations

Dextran was given to 29 patients undergoing more or less severe surgical operations. The amounts given were as follows: 13 patients received one bottle (540 ml.), 13 received two bottles, 1 received three bottles, and 2 received four bottles. The rates of infusion varied from 200 ml. in 2 min. to 540 ml. in 6 hours (by slow drip), and the ages of the recipients ranged from 8 to 81 years.

It was appreciated at the outset that it would be difficult in such a trial to obtain decisive evidence of the value of dextran compared, for example, with that of blood or of plasma. Nevertheless, the results obtained have been very promising, as will be seen from the following representative examples:

Case 1.—Male, aged 41. On June 1, 1948, partial gastrectomy was done for chronic peptic ulcer, 500 ml. of whole blood and 1 litre of saline solution being given during operation. Next day the patient's condition was satisfactory. On June 3, 48 hours after operation, after drinking a little water, he suddenly developed upper abdominal pain and collapsed. On examination 80 min. later he was restless and his skin cold and clammy; pulse-rate 104, pulse volume poor; blood-pressure (B.P.) 136/104. His blood showed evidence of slight hæmoconcentration (hæmatocrit reading 54 c.cm. per 100 ml., Hb 112%). Leakage at the gastrectomy suture line was diagnosed, and an infusion of dextran (GL/50/3) was started. After 540 ml. had been given in just over an hour, the pulse had become stronger, and the patient was a little warmer; B.P. 132/90. After a further 250 ml. of dextran in another hour the B.P. was 162/106, and the patient's pulse was now good. He had become more wide awake, having previously been lethargic. The hæmoglobin percentage had fallen from 112 to 96. The

TABLE I—DEXTRAN CONCENTRATION IN RABBIT TISSUES

Tissue	Rabbit 1 (control)		Rabbit 2		Rabbit 3		Rabbit 4		Rabbit 5		Rabbit 6	
			Days after injection									
	Chem. (mg./g.)	Serol.	2		9		21		35		56	
			Chem. (mg./g.)	Serol.	Chem. (mg./g.)	Serol.	Chem. (mg./g.)	Serol.	Chem. (mg./g.)	Serol.	Chem. (mg./g.)	Serol.
Liver	ND	0	0·3	+ + +	0·2	+	ND	+ +	ND	? +	ND	+
Kidney	ND	0	0·2	+ + +	0·3	+	ND	+	ND	? +	ND	+ +
Cervical lymph-gland	ND	0	2·3	+ + +	2·5	+ + +	1·6	+ + +	ND	+	D	+
Mesenteric lymph-gland	ND	0	1·5	+ + +	2·3	+ +	1·4	+ + +	ND	+ +	ND	+
Popliteal lymph-gland	ND	0	—	+ + +	5·0	+ +	D	+ + +	D	+ +	ND	+
Spleen	ND	0	2·0	+ + +	1·4	+	1·4	—	ND	+ + +	ND	+ +
Muscle	ND	0	0·2	+ +	0·6	+	ND	+	ND	+	ND	0
Plasma	ND	0	10·4	+ + +	5·2	+ +	0·5	—	0·5	+ +	ND	0

Chem., dextran concentration in mg./g. estimated by chemical method: D, detected; ND, not detected; —, not tested.
Serol., presence of dextran tested for by serological method: +, positive result; 0, negative result; —, not tested.
Animal 6 received dextran 6·1 g. per kg. of body-weight, comparable with a transfusion of 1 litre a day for 7 days in the average adult.

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patient was considered fit for operation, and under thiopentone and cyclopropane anæsthesia laparotomy was performed. The peritoneal cavity contained just under 500 ml. of free fluid. The gastric wall at the site of the previous anastomosis was excised and gastro-enterostomy was redone.

A further 540 ml. of dextran was given during the latter part of the operation, and this was followed by intravenous glucose-saline solution. No other intravenous therapy was given. The patient's condition remained satisfactory and he made a complete recovery.

This patient developed signs of peripheral failure following leakage of stomach contents from a breaking down gastric operation wound. His circulation was greatly improved after administration of about 1 litre of dextran, and the administration of a further $^1/_2$ litre enabled him to withstand a second operation without redeveloping any signs of peripheral failure. He made a good recovery. A firm impression was left that only the transfusion of whole blood or of plasma could have produced a similar result.

Case 2.—A man, aged 46, had malignant hypertension with a resting B.P. of 245/130. On July 20, 1948, transthoracic lumbar sympathectomy was done. During the operation his B.P. began to fall, and an infusion of 540 ml. of dextran (GL/50/3) was begun. There was very little bleeding during the operation, but the blood-pressure continued to fall to 94/56. A further 540 ml. of dextran was infused over the next 4 hours, and the B.P. was by that time remaining at about 120/70. Dextran was now discontinued, and a saline-solution drip was given. The B.P. immediately fell again, and in 4 hours had reached 80/58. At this point a third amount of 540 ml. of dextran was infused in 2 hours, producing a rise in B.P. to 110/70, and a fourth bottle in $3^1/_2$ hours still further increased the B.P. to 154/112. The B.P. was taken hourly over the next four days and remained stationary at 146/84. There was no further fall, and the patient made a good recovery.

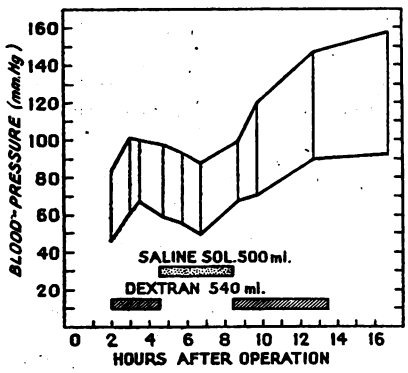

Fig. 3—Effects of two postoperative injections each of 540 ml. of dextran and of 540 ml. of saline solution on blood-pressure (case 3).

A considerable fall in blood-pressure in a patient undergoing sympathectomy for malignant hypertension was successfully restored with dextran. When the dextran was discontinued, and saline solution infused in its place, the B.P. fell again and continued to fall to a dangerously low level. Further amounts of dextran were given, and the B.P. rapidly rose again. No further fall took place, and the patient made a good recovery and about two months later walked home. In this case again the impression was gained that in the restoration and maintenance of the B.P. dextran was an infusion fluid superior to saline solution. This impression was further substantiated by the next case.

Case 3.—A man, aged 81, poorly nourished and helpless, had chronic bronchitis, emphysema, and carcinoma of the rectum. He was in hospital for two months, during which time measures were taken to improve his general condition and nourishment before he was considered fit to undergo colostomy and perineal resection of the rectum. His hæmoglobin concentration before operation was 16·1 per 100 ml. Operation was successfully carried out, 1 litre of whole blood being given during the procedure, and the patient returned to the ward in good condition. After 2 hours, however, he became cold and clammy, his pulse was thready, and his B.P. was 84/45 (fig. 3). Dextran (GL/50/3) was infused, and after 250 ml. had been given in 45 min. the B.P. was 102/60. The patient's general condition had greatly improved, and a further 290 ml. of dextran was given by drip over a period of 2 hours, followed by a saline-solution drip. Saline solution was given over a period of 4 hours; the B.P. fell gradually, the patient's condition grew worse, and his skin became cold to touch. Consequently a further 540 ml. of dextran was infused, and this produced a rapid and sustained rise in B.P. The jugular venous pressure had also risen to +1 cm. by the end of this infusion; and, to avoid any overload, intravenous therapy was discontinued at this point. The B.P. did not fall again, and the patient improved rapidly.

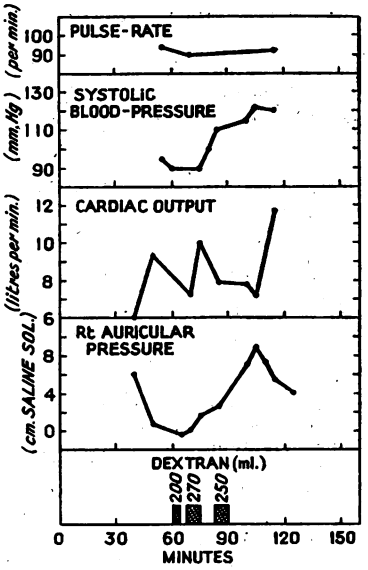

Fig. 4—Effects of injections of dextran on right auricular pressure, cardiac output, and systolic blood-pressure during operation (case 4).

Intravenous dextran rapidly restored and maintained the B.P. in an elderly patient who had undergone a severe operation. This case again emphasised the necessity to note carefully the state of venous filling to avoid circulatory overloading when infusing dextran, especially in an elderly person.

Further information on the effect of dextran infusion on the venous filling pressure and cardiac output was obtained in two patients studied with the cardiac catheter during operation. Right auricular pressure (R.A.P.) was measured with a saline-solution manometer, and cardiac output by the Fick principle, by the methods already described by McMichael and Sharpey-Schafer (1944) and Sharpey-Schafer (1944).

Case 4.—A woman, aged 65, had had jaundice and intermittent abdominal pain for four months. Obstructive jaundice was diagnosed, choledochostomy under nitrous oxide and ether anæsthesia was done, and a large single cholesterol stone was removed. The bile-duct was drained. Fig. 4 is a graphic record of measurements made in a cardiac catheter study during the operation, which lasted 125 min. The R.A.P., cardiac output, and B.P. fell towards the end of the first hour, and dextran (GL/50/3) was given through the catheter in amounts of 200 ml., 270 ml., and 250 ml. in $4^1/_2$, 7, and 7 min. respectively. The R.A.P., cardiac output, and B.P. each showed a satisfactory rise. The R.A.P. continued to rise for several minutes after administration of

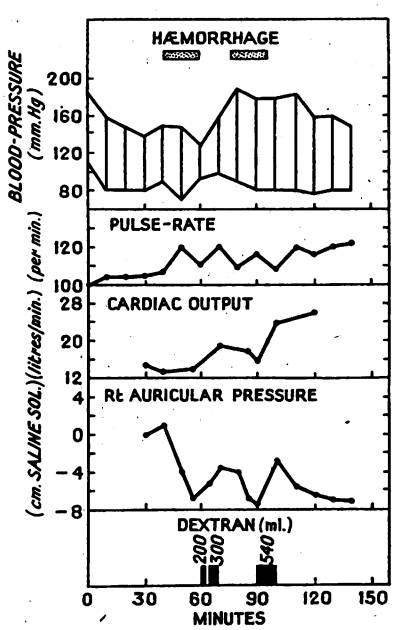

Fig. 5—Effects of injections of dextran on right auricular pressure, cardiac output, and blood-pressure during operation associated with hæmorrhage (case 5).

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TABLE II—PLASMA-DEXTRAN LEVEL SOME HOURS AFTER INJECTION

Case no.	Total amount of dextran infused (g.)	Duration of infusion (hours)	Plasma-dextran level (g. per 100 ml.)	Time after infusion of first plasma sample (hours)
8	68	7½	0·88	1
4	44	½	1·25	3
2	136	20	1·8	1
9	68	4	1·05	8
3	56	12	1·19	5
10	134	40	0·94	22

dextran, probably because dextran has a greater osmotic pressure than blood.

The operation was completed, and the patient returned to the ward in excellent condition. Postoperatively there was no fall in B.P., and convalescence was entirely uneventful.

Case 5.—A man, aged 56, with gastric carcinoma underwent splenectomy and subtotal gastrectomy under nitrous-oxide, oxygen, and ether anæsthesia. His B.P. before operation was 190/100, and catheter measurements were made during the operation. On two occasions (fig. 5) during the operation a very brisk hæmorrhage caused a fall in R.A.P., cardiac output, and B.P. Dextran (GL/50/3) was given as follows: 200 ml. in 2 min. and 300 ml. in 4 min. on the first occasion; and 540 ml. in 8 min. on the second. On each occasion the R.A.P. and cardiac output were successfully restored and the B.P. maintained. The operation lasted 140 min. and was completed successfully, but by the end the R.A.P. had begun to fall again. Further resuscitation was carried out by means of whole-blood transfusion in view of the severe blood-loss, and the patient recovered.

In this case dextran was used to restore the venous filling pressure and maintain the B.P. when these were falling during hæmorrhage.

Plasma Levels of Dextran

The postoperative patient is not the ideal subject in whom to estimate serially plasma-dextran levels, since these levels are modified by exudation into wounds and, in many instances, by the need to administer intravenous crystalloid fluids. However, plasma-dextran has been estimated in 7 patients for periods of two to seven days, and approximate information about the rate of disappearance of infused dextran from the blood has been obtained. About a third of the dextran present at a time disappears during the next 24 hours. In table II a few details are given of 6 cases in which the plasma-dextran level was estimated at intervals after infusion. It will be noted that the first sample was often only obtained many hours after infusion, and the plasma-dextran level observed was doubtless lower than the maximum attained. However, the observed figures have been taken as 100%, and plasma-dextran levels observed subsequently have been expressed as percentages of these figures. In fig. 6 the serial plasma-dextran levels in 6 patients are plotted as percentages of the maxima against time. These percentages are shown on a logarithmic scale, and the corresponding straight line for one-third decrement per day is put in for comparison.

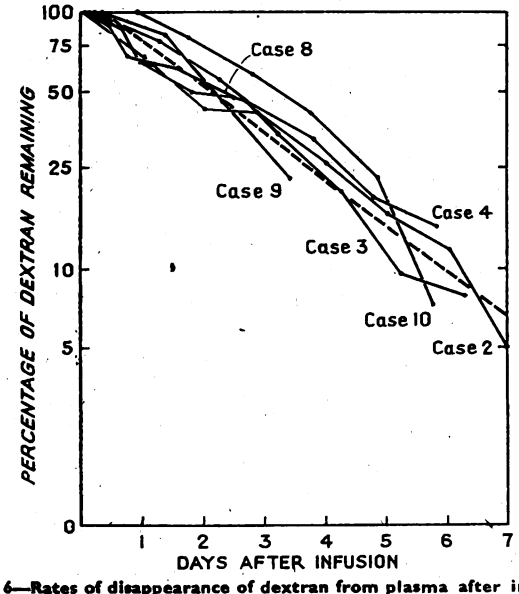

Fig. 6—Rates of disappearance of dextran from plasma after infusion in 6 cases; interrupted line representing a third decrement a day has been inserted for comparison.

Plasma-protein and Plasma-dextran Levels

In 3 cases the plasma-protein and plasma-dextran levels were measured in serial plasma samples. It was found that the plasma-protein level was reduced after the infusion of dextran and slowly rose again as the dextran was eliminated. Thus the total of protein + dextran tended to remain constant. An example is given in fig. 7.

Renal Excretion of Dextran

Eight-hourly urine collections were made in 7 cases over periods of two to five days after dextran infusions, and the dextran content was estimated. The total amount recovered varied from 9 to 26% of the total amount infused. In 6 out of 7 cases the concentration in the urine had fallen to a low level by the end of 48 hours after the infusion, but in one case an appreciable amount was still being excreted on the fifth day. One result is illustrated in fig. 8, in which the total amount of dextran excreted in serial 8-hour samples has been recorded. In this case 30 g. of dextran was infused into a patient with carcinoma; 7·35 g., 25% of the total, was excreted in the urine, and half of this amount came out within 8 hours of the infusion. This case has been chosen for illustration because this patient, unlike the others, had not just had an operation.

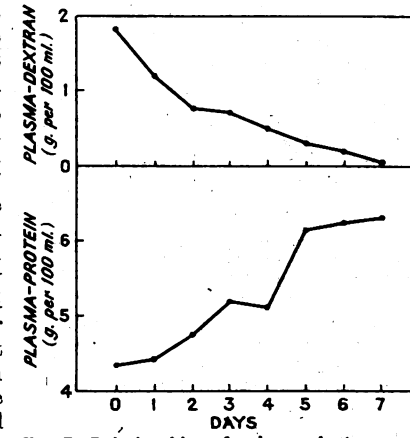

Fig. 7—Relationship of plasma-dextran and plasma-protein levels during seven days after infusion of dextran 130 g.

In another patient, in whom the common bile-duct was drained for ten days after operation, there was an opportunity to see whether dextran was excreted in the bile. Though the plasma-dextran level exceeded 1 g. per 100 ml. during the relevant period, no dextran was detected in the bile.

Reactions to Infusion

During these trials no pyrexia reactions followed dextran infusions, nor were there any subjective complaints either of a general nature or of local pain at the site of infusion. Urticaria was not seen. Finally, there was no instance of venous thrombosis or thrombophlebitis among the cases.

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Follow-up

Some months after receiving dextran 6 of the patients were recalled to hospital. All but 1 appeared healthy. The exception, who had a dissecting aneurysm of the abdominal aorta, was in poor health and had albuminuria. Nothing abnormal was found in the urine of the remaining 5. Clinical examination of all 6 revealed no change in size of liver or spleen, no enlargement of lymph-glands, and no alteration in B.P. Blood examination showed no lowering of hæmoglobin percentage or of serum-protein level, and no increase in serum-bilirubin. Dextran was not detected in the plasma either by chemical tests or, in 5 of the 6 cases, by the very sensitive serological method. In the 6th case the test was only very doubtfully positive.

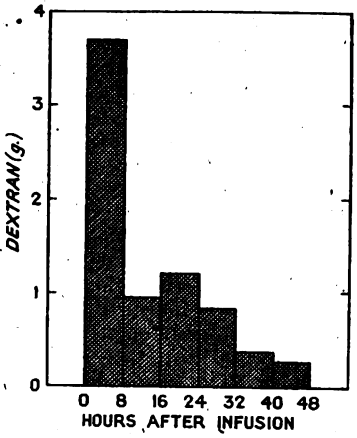

Fig. 8—Excretion of dextran in urine in 8-hour periods after infusion of dextran 30 g.

Patients with Burns

Plasma has for some time been regarded as the most suitable transfusion fluid for patients with extensive burns, and units treating burns have considerable experience of the effects to be expected from plasma-transfusion. It was thus felt that cases with severe burns would be particularly suitable for assessing the value of dextran. It was given to 2 patients who would otherwise have had plasma.

Case 6.—A boy, aged 8, burned the whole of his right leg and was admitted to the burns unit an hour later in fairly good general condition, a little cyanosed, and with cold extremities and a pulse-rate of 80. An hour after admission the venous hæmatocrit reading was 41 c.cm. per 100 ml. and the pulse-rate 88. An intravenous dextran drip (batch GL/50/2) was started (fig. 9): 200 ml. of dextran was given in the first hour, and 100 ml. in the next hour; by the end of 2 hours' infusion the boy's general condition was very good. His feet were warm, and his colour was much improved. The hæmatocrit reading was 39 c.cm. per 100 ml. and pulse-rate 80. The drip was now slowed to a rate of 50 ml. an hour.

Plenary dressing was done 4 hours after the start of the infusion; the burnt area was estimated to be 15% of the body surface, the burn being almost entirely superficial. The dressing operation lasted an hour, and the patient's condition remained very good throughout. At the end the pulse was of good volume, rate 90, and the hæmatocrit reading 42. By that time 450 ml. of dextran had been given. The rate of flow was then increased to about 75 ml. an hour, and 4 hours later the hæmatocrit reading had fallen to 38. The rate of flow was again reduced to about 50 ml. an hour, and the hæmatocrit reading four hours later was 40.

Throughout this time the good condition of the patient was well maintained. He was taking fluids freely by mouth and was passing large quantities of urine. The dextran drip was discontinued 18 hours after its start, a total of 1080 ml. (≡ 69 g. of dextran) having been given. Urine specimens continued to be collected 8-hourly, and samples of blood were taken at increasing intervals.

A slight pyrexia—99–100°F—had begun during the first day and continued for nine days. This is a common finding in burned patients. Otherwise the patient's general condition was excellent. His hæmatocrit reading, after rising to 44 on the day after cessation of the transfusion, fell slowly to 37 four days after the accident; thereafter it showed no further change. The hæmoglobin was 11·9, 12·1, and 11·9 g. per 100 ml. on the fourth, seventh, and fifteenth days after burning. A complete clinical examination made on the eighth day showed no abnormalities; no abnormality was detected in the urine, and the blood-urea was within normal limits (25 mg. per 100 ml.) The areas of full-thickness skin-loss, which were grafted on the nineteenth day, took just as well as in comparable patients resuscitated with plasma. When seen three months after the injury the boy had been playing games and was in excellent condition.

Plasma-dextran Levels.—A maximum of more than 2 g. of dextran per 100 ml. of plasma was reached at the end of the infusion (fig. 9). This gradually declined by about a third per 24 hours, with the result that 1 g. of dextran per 100 ml. was still present 60 hours after the start of the infusion. Only a trace of dextran remained in the plasma after ten days.

Plasma-protein Levels.—From an initial value of about 5·7 g. per 100 ml. the plasma-protein level fell to 3·3 g. per 100 ml., when the plasma-dextran level was at its highest. As the dextran later disappeared the protein returned, with the result that the total colloid was maintained at about 6 g. per 100 ml. The protein had regained normal values by the fourth day after the transfusion.

Urinary Excretion of Dextran.—Dextran appeared in the urine within an hour of the start of the infusion. A fifth of the weight of dextran infused was excreted, and most of this came out within a few hours of ending the infusion.

Intravenous dextran given to this patient with fairly severe burns provided a satisfactory substitute for plasma transfusion. Its effect in counteracting hæmoconcentration was clearly demonstrated, and a plasma-dextran level rising to 2 g. per 100 ml. was tolerated without evidence of ill effects either immediate or remote; the dextran only disappeared slowly from the plasma after infusion.

Case 7.—A woman, aged 42, received severe burns when her clothes caught fire. She was admitted to the burns unit two hours later, severely shocked, cyanosed, and with cold extremities and an imperceptible pulse; the venous hæmatocrit reading was 60 c.cm. per 100 ml.

Within half an hour an intravenous infusion of dextran (GL/50/2) was started, and half an hour later, when 1 litre had been given, the pulse became palpable at the temple. The hæmatocrit reading had now fallen to 44, and with the improving circulation the morphine gr. $^1/_2$, which had been given before the patient's admission, began to take increased effect. The respiration-rate was depressed to 12 per min. and fell during the next hour to 8 per min. In the first 3 hours of infusion 3 litres of dextran was given, and hæmoconcentration was well controlled. About this time there was trouble with vomiting, which continued to interfere with the administration of fluids by mouth for the next 15 hours. The intravenous dextran was continued for 24 hours, 4540 ml. (≡ 288 g. of dextran) being given in all. The drip was then continued with 1 litre of saline solution given during the next 24 hours. The patient's

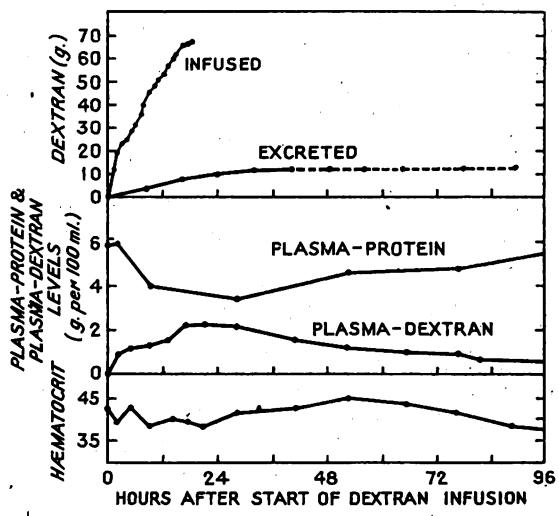

Fig. 9—Hæmatocrit, plasma-protein and plasma-dextran levels, and infusion and excretion of dextran in boy with extensive burns (case 6).

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general condition improved, and she began to take more interest in her surroundings. Regular blood samples were obtained, though the extensive burns made choice of site difficult. Urinary output was low during the first two days.

The plenary dressing was done on the second day after admission. Full-thickness burns were found on all limbs, and partial-thickness burns as well on the back, face, neck, and chest. All these areas were very œdematous. A total of 50% of the body surface was affected—40% deep, and 10% superficial burns. Despite prophylactic systemic penicillin, the burns became infected.

After the vomiting had ceased on the first day of treatment, the patient took fluids well by mouth: 5 litres was given on the second day, and 4 on the third. The output of urine then improved. At this time respirations were normal and the extremities were warm. A moderate pyrexia superseded the abnormally low temperatures recorded in the earlier stages. Hæmatocrit readings were 33–37.

On the fourth day there was little change. The hæmoglobin percentage and hæmatocrit reading were both low, as would be expected during the reabsorption of the œdema fluid, and blood-transfusion was arranged for the following morning. During the night the patient's condition deteriorated. At 6 A.M. on the fifth day the temperature had risen to 102°F, the respirations were 38 per min., and the pulse, which was of poor volume, had a rate of about 50. No adventitious sounds were heard in the chest. The patient began to be irrational. Blood-transfusion was started, and oxygen was given by B.L.B. mask. 1300 ml. of blood was given, but the patient became increasingly comatose, and her temperature continued to rise. In the afternoon, 114 hours after admission, she died. Blood-culture taken at death yielded *Pseudomonas pyocyanea*.

It is uncertain what determined the deterioration in the final 12 hours. The hæmoconcentration of the shock phase had been satisfactorily corrected; the plasma-protein level was rising to normal values, and urinary output was improving. Reabsorption of œdema fluid was taking place; hence overloading of the circulation might have been a factor. Against this, the symptoms were of cerebral type, and no abnormal chest sounds were heard. Toxic absorption from the very large infected burn seems the most important feature.

Necropsy (Dr. S. Sevitt) showed œdema and congestion of parts of the lungs and evidence of raised intracranial pressure. Histological examination of the liver showed a widespread non-hæmorrhagic necrosis. The kidney tissues were œdematous, and there was desquamation of cells lining Bowman's capsule and the loop of Henle. The appearance of the liver may have been due to post-mortem autolysis. The cause of the kidney changes remains in doubt.

Plasma-dextran Levels.—A maximum of 4 g. of dextran per 100 ml. of plasma was reached. This declined fairly rapidly, possibly by loss into the œdema fluid, to about 1·5 g. 24 hours later, and then more slowly, as in case 6, at the rate of a third per day.

Plasma-protein Levels.—Corresponding to the high levels of dextran, the plasma-protein levels became very low and for 30 hours were less than 2 g. per 100 ml. The proteins returned as the dextran disappeared and were almost normal when death occurred. No harmful effects of the changes in plasma-protein level were noted, and by the fifth day most of the œdema fluid of the burns had been reabsorbed.

Urinary Excretion of Dextran.—In spite of the reduced urine volumes, the excretion by weight of dextran was very similar to that in case 6. About a sixth of the infused dextran was recovered from the urine, and again most of this came out within a few hours of the infusion. A maximum of 13% dextran was found in the urine, showing that dextran can be concentrated at least threefold by the kidney. This urine sample was notably viscous. Estimation showed that the excreted material consisted of the smaller molecules in quantities corresponding to their presence in the solution transfused.

The infusion of large volumes of dextran in this case of very severe burns demonstrated its adequacy for volume replacement and for the maintenance of osmotic pressure. The detailed cause of death remains in doubt, but the burns in themselves, could easily have been fatal. There was no evidence that dextran contributed to the fatal outcome.

DISCUSSION

The degree to which dextran fulfils the theoretical requirements laid down above can now be discussed.

Dextran is well retained in the circulation, and our observations show that it can maintain the osmotic pressure until its place is taken by the plasma-proteins. The slow rate of disappearance of dextran from the plasma shows that it does not pass rapidly into the tissues. However, a significant proportion, amounting to some 25% in most of the batches tested, does escape into the urine soon after infusion. In one case it was possible to demonstrate that the dextran escaping into the urine was of lower molecular weight than the average of the dextran infused (cf. Bohmansson et al. 1946). It is clear that the greater the proportion of dextran of molecular size which will pass the glomerular filter, the less the value of dextran as a substitute for plasma becomes. On the other hand, Grönwall and Ingelman (1945a) have found that, if the molecular weight of dextran is insufficiently reduced during the stage of acid hydrolysis, the resulting product causes renal damage. Thus it is desirable to prepare dextran with a defined range of molecular size. Further, a uniform preparation is required if reproducible clinical effects are to be obtained. At present details of a specification are being worked out in collaboration with the manufacturers. Limits for the range of molecular size and for the mean will be defined by practical physicochemical tests; and there will probably be further biological criteria depending on injections into animals. Such a specification should ensure a standard of consistent physiological efficiency not hitherto attained in a fluid used for artificial resuscitation. In developing this specification it will probably be best to lower slightly the total content of sodium chloride and dextran; in the experiments on animals it was noted that restoration of blood-pressure was more rapid after dextran infusion than after blood-transfusion; and in the clinical trials a secondary rise in blood-pressure after the infusion of dextran was sometimes observed, suggesting that fluid was being drawn into the circulation.

Though dextran appears to possess the positive qualities required of a plasma substitute, one important doubt remains on the negative side—namely, the ultimate fate of dextran in the body. No evidence has been obtained to support or disprove the statements of Grönwall and Ingelman (1944, 1945a and b) that dextran is metabolised, probably as glucose. The experiments in which dextran was incubated with extracts and suspensions of liver and pancreas indicate that its degradation in the body is unlikely to be rapid. In rabbits injected with dextran, the dextran remaining in the body, after the excretion by the kidney of the material of small molecular weight, passes into the tissues, particularly into the reticulo-endothelial system. In the course of eight weeks, under the conditions of these experiments, the concentration falls gradually, but even at the end of this period dextran can still be detected by the serological method, especially in the lymph-glands and spleen, when it can no longer be detected in the plasma. This evidence suggests that dextran gradually disappears from the body, but a definite statement cannot be made until further experiments have been made to show whether its disappearance is complete.

Several possibilities regarding the fate of dextran in the body suggest themselves:

(1) The retained polysaccharide may be broken down slowly and metabolised as glucose. Swanson (1948) has shown that undegraded dextran is resistant to α and β amylase, muscle, and potato phosphorylase. The 1–6 linkage, which predominates in dextran molecules (Fairhead et al.

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1938, Peat et al. 1939, Hassid and Barker 1940), appears to resist enzymic hydrolysis, or perhaps the configuration of the molecule is such that enzymic action is inhibited; but this does not necessarily mean that degradation in the body will not eventually take place.

(2) The retained polysaccharide may be slowly broken down to a molecular weight less than 70,000 and excreted by the kidneys.

(3) Part of the retained polysaccharide may be excreted after suitable degradation, the remainder being burnt as glucose.

The fate of the retained material is of great importance, for the ideal substitute for plasma should be completely metabolised or excreted. Until its fate in the body is known, dextran cannot unreservedly be recommended as a substance for intravenous infusion. With this proviso, a dextran solution with the characteristics described appears to be free from the disadvantages of other non-protein substitutes for plasma.

SUMMARY AND CONCLUSIONS

It is possible to prepare dextran with a range of molecular size similar to that of the plasma-proteins. The solution is well tolerated as an infusion by man and is not pyrogenic, toxic, or antigenic.

Such dextran, after infusion into animals and man, is only slowly removed from the plasma over about a week.

Dextran has proved efficacious as a plasma substitute in cases of burns, and has produced a sustained increase in the venous return in patients with surgical shock or hæmorrhage.

The dextran under trial has contained an appreciable proportion of material of such a molecular size that it passed the glomerular filter and could be recovered from the urine. In defining a specification for dextran for intravenous use it is clearly desirable to keep to a minimum the proportion of dextran of low molecular weight. It is probably also important to define the upper limit of molecular size.

There is still doubt about the ultimate fate of dextran in the body. Because of this, dextran cannot yet be unreservedly recommended for widespread use. Nevertheless, in the investigation made in this trial, it has not been shown to produce any harmful effect on the tissues, and further investigation is recommended.

We would like to thank Mr. W. Gissane, clinical director, Birmingham Accident Hospital, Mr. Dallas Ross, M.R.C. Burns Unit, and Prof. Ian Aird and Mr. R. H. Franklin of the department of surgery, Postgraduate Medical School of London, for permission to treat cases; and the East Anglian Chemical Co., Aycliffe, co. Durham, for their coöperation and the generous gift of dextran.

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EFFECTS OF AGENISED FLOUR ON MAN

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WHEN this investigation started, 'Agene' (nitrogen trichloride) had been in use as an improver for flour for over 25 years. No reports had been published, however, on the effect this process might have on the nutritional value of flour for man. In 1946, Sir Edward Mellanby showed conclusively that the agenisation of flour rendered it highly toxic to dogs. A further paper (Mellanby 1947) showed that ferrets were also susceptible to the toxin, and that this was associated with the protein of the flour. It therefore seemed worth while undertaking a survey to find out if any effects attributable to agenised flour could be detected in human beings.

Since the agene process has been current commercial practice for so long, it is improbable that it could be a direct cause of major illness; but, in view of the serious reaction produced in dogs, the lack of knowledge of the reversibility of any changes which might occur, and the absence of a suitable antidote, it was considered unethical to feed super-agenised flour to human subjects. It was therefore decided to compare a group of children fed on the current agenised flour with a group from whose diet all flour products treated with agene had been removed. With the coöperation of the local authority concerned such an investigation was undertaken in a residential school.

The sample on which the survey was made was not representative of the general population because almost all the children came from homes which were social failures; they were, however, free from gross physical or mental defects. To detect minimal changes a large homogeneous group was required. This was not available; the ages of the children at the school ranged from 2 to 15 years, they were of either sex and were diverse in their intellectual and temperamental potentialities, and about a third of them were admitted only for short periods. It was also important that the two groups should have the same psychological background. If the groups were under the care of different house-mothers or different masters, differences in behaviour, to be significant, would have to be unequivocably the result of organic lesions. There was left, eventually, a group of 80 boys aged 10–15 years, living in two houses, P and Q, but taking all their meals in one main dining-hall. These boys were paired for age and intelligence, and two groups were selected, both houses contributing half their inmates to each group. This artificial grouping only appeared at meals; at all other times the boys mingled indeterminately, either in class or house. Most of the observations were made on the children from these two houses, and the results reported refer to them unless otherwise stated. These two groups received identical diets, except that group A received flour agenised at 8 g. to the sack (3·2 g. per cwt.), and group X flour which had not been agenised. During the investigation, dietary surveys revealed no constant variation between the food intake of the two groups apart from the difference in flour. The remaining children in the school ate in their own houses and similarly received either agenised or unagenised flour.

The original plan of the investigation was to remove a group of children from the effects of agene for six months and then to compare them with a control group. Positive results were then to be checked by reversing

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the diets for a further six months. At the end of the first period, however, no constant or significant differences were detected between the two groups, and it was decided to abandon the investigation. However, about this time it was discovered that the commercial treatment of flour sometimes reached the level of 12 g. to the sack (4·8 g. per cwt.). Further, though it seemed possible that the toxic action of agenised flour might be slowly cumulative, it was just as likely that, as with other organic pharmacologically active compounds, the subject might develop considerable tolerance. It was therefore decided to try the effect of agenised flour on the group that had lived for six months without it. Considerable difficulty was experienced in obtaining sufficient quantities of the flour agenised at 12 g. to the sack, and this part of the investigation lasted only six weeks.

It was impracticable to test all the children before the investigation proper began, and most of the tests were administered at the beginning and end of the main period. Subsequently, adequate control figures were obtained after the final switch-over. For the purposes of reporting and assessing the results the investigation has been divided into four periods:

(1) Before the separate diets started, June 12 to July 14.
(2) First part of the main period, July 15 to Dec. 20.
(3) Second part of the main period, Dec. 27 to March 10.
(4) Control period when the diets were reversed, March 11 to April 24.

NATURE OF INVESTIGATIONS

The knowledge that excessive doses of agenised flour in dogs cause ataxia, disorientation, and epileptiform fits together with hæmorrhagic lesions in the intestines, gave little indication of the effects that were to be expected in man. It was therefore decided to test as wide a range of functions as possible—i.e., growth, general health, coördination and motor ability, intellectual performance, and temperament and behaviour.

Growth

Before the experiment started, the height and weight of each child were recorded. During the investigation, except in two houses, each child was weighed fortnightly unless he was sick, on holiday, or absent without leave. Weights were recorded to the nearest ounce, without clothes, and at the same time of day. Weight gains and losses, besides reflecting growth and indicating general health, are unfortunately affected by many other factors, among which are age, initial weight, puberty, intercurrent illness, amount of exercise, hydration, attractiveness of diet, and climatic conditions. All these variables were present, and the total variability is so great that the detection of small differences between the groups becomes very difficult.

Two observations were reported. In houses P and Q a small group of 34 boys were paired for original weight, and their weight gain calculated for the main experimental period (2 and 3). The mean original weights were 5 st. 5 lb. 4 oz. for both the agenised-flour group and the unagenised-flour group. The former group gained on the average 6 lb. 1 oz. and the latter 8 lb. The difference is not significant ($t = 1·7$, $P > 0·1$).

After reversal of the diets, the mean daily gain for a month before and for a month after the change has been calculated for 151 children of either sex and various sizes. The difference in rate of gain between these two periods has been calculated for each child. Both groups showed a fall in growth-rate during the second period. For the 76 children changing from agenised to unagenised flour the rate fell from 0·590 oz. to 0·417 oz. a day ($d = 0·173$), whereas for the group changing to agenised flour the fall was from 0·648 to 0·261 oz. a day ($d = 0·377$). These differences between the groups are not significant ($t = 1·54$, $P > 0·1$). Agenised flour, therefore, has not been shown to affect weight increase significantly, either over eight months or after a sudden change of diet.

General Health

The children were examined clinically before the investigation started. Subsequently, records were kept of all those reporting sick. The examination, diagnosis, and treatment of these children remained in the hands of the school medical officer and his staff. These records were analysed to obtain the total number of minor infections contracted by each group. "Minor infections" included colds, sore throats, coughs, styes, and boils. No child was counted as having a second infection unless there had meantime been at least a week's clear health. There was no significant difference between the groups.

In addition to this analysis of the records, the children were examined on several occasions for changes in their deep reflexes and were also given short clinical tests of coördination and balance. No symptoms or signs were detected which could be attributed to intoxication with agenised flour. Dr. Bruce White kindly examined 57 specimens of fæces and detected no change in the predominant bacterial flora. Tests for occult blood were negative. Further evidence that the health of the children was not greatly impaired was provided by their performance in the agility test, for performance

TABLE I—RESULTS OF PSYCHOMOTOR TESTS

Test	No. of boys in group	Method of scoring	Standard deviation of scores (1st run)	Test and retest reliability (r)	First part of main period	Second part of main period	Control period
Tremor	R, 39 S, 34	No. of holes successfully negotiated in 9 attempts	6·3	0·70	R, 22·97 S, 21·18	R, 25·05 S, 21·68	R, 27·87 S, 26·67
Simple finger	R, 38 S, 34	No. of pegs turned in 35 sec.	3·7	0·59	R, 63·89 S, 62·53	.. ..	R, 73·57 S, 70·06
Triple tester	R, 39 S, 37	No. of successes	21·9	0·51	R, 82·85 S, 80·59	R, 113·18 S, 110·89	..
Hand, foot, and eye coördination	R, 39 S, 38	No. of errors	12·9	0·68	R, 128·33 S, 126·28	R, 82·95 S, 83·22	R, 43·15 S, 46·06
Agility	R, 31 S, 27	Speed of performance (sec. taken for one run)	7·7	0·63	R, 97·57 S, 98·58	R, 95·88 S, 97·68	R, 97·71 S, 96·57
Beam	R, 37 S, 35	Endurance of test conditions (sec.)	71·8	0·53	..	R, 126·41 S, 118·12	R, 124·70 S, 120·50

During both parts of the main period group R received agenised flour, group S unagenised flour. During the control period group S received agenised flour and group R unagenised flour. Results are expressed as the mean scores for each group. The difference between means is not shown in the table. In no case did this difference exceed a chance probability of 1 in 20.

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on this test is readily affected by minor ill health (Frankau 1943).

Coördination and Motor Ability

In addition to clinical examination, a record was kept of the children's performance in organised games and sports. Members of the cricket, football, and swimming teams did not appear to be adversely affected by either diet. Nor did dietary factors play any part in determining the results of the annual sports. The children were also examined with a battery of psychomotor tests. These tests were selected to form a scale of increasing complexity. All of them have been described elsewhere; though the details of administration were varied to render them suitable for the children, this never materially altered the character of the tests. The tests used were:

TABLE II—RESULTS OF INTELLIGENCE TESTS

Group of children	Mean standardised score in:	
	Jenkins non-verbal intelligence test (June, 1947)	Raven's matrices (December, 1947)
R: 30 children receiving agenised flour	96·3	96·3
S: 22 children receiving unagenised flour	93·4	91·9

Test-retest correlation for both groups: r = 0·67.

(1) Tremor test of hand steadiness. This consisted of passing a rod 3 mm. in diameter through holes of various sizes without touching the side. For a detailed description of a similar test see Halstead (1947).
(2) Simple finger dexterity (R.A.F.*).
(3) Hand and eye coördination: triple tester.†
(4) Hand, foot, and eye coördination: S.M.A. 3 (R.A.F.*).
(5) Agility (Frankau 1943).
(6) Beam test (Milligan 1934). In this test the subject hangs for as long as possible from a beam.

In testing the children it was not possible to see that every child did each test every time. To take only those children who underwent all the tests would make the groups very small. On each test, therefore, the results reported are for a group of children who were present every time that particular test was repeated. The children coöperated extremely well in the tests; their association with pilot-selection was emphasised, and they were presented on a competitive basis. In practically all the children excellent motivation was obtained. On the second occasion that the beam test was used additional rewards were offered, but only a slight increase in motivation was noted.

The results of these tests are as follows: on most of the tests the group receiving agenised flour was definitely superior, but the differences between the mean scores of the two groups never reached a statistically significant level. It is worth noting that, on repeated testing, the group receiving agenised flour generally showed the most improvement. The average improvement for each group was calculated, but again the differences never reached an acceptable level of significance. To estimate the significance of the differences between means the t test was used (Fisher 1946). The results of those tests are presented in table I.

Intellectual Performance

Before the experiment started, the children were given a formal group test of intelligence. Cheating was rigorously precluded. Six months later another test was administered. Since many of the children could neither read nor write with much facility, tests were chosen which had no written verbal element. The two tests finally used were the Jenkins non-verbal test of mental ability (Jenkins 1947) and Raven's matrices (Raven 1940). There was no impairment in either group. The results of these tests, expressed as mean standardised scores (equivalent to an intelligence quotient), are given in table II.

Temperament and Behaviour

Considerable difficulty was encountered in obtaining objective evidence of changes in temperament and behaviour. The results of the formal tests would be affected by any gross increase in irritability, distractability, or impaired concentration, but no such effect could be detected. However, none of these tests can be described as primarily a test of temperament. The beam test and the agility test seem those most likely to be affected by poor coöperation, and both these tests were, if anything, accomplished better by the children receiving agenised flour. Ratings of behaviour in class, which were kindly carried out by the teaching staff, merely revealed the chronic offenders, and did not show any difference between the two groups.

The most objective investigation practicable in this field is an analysis of the school record of punishment for boys in houses P and Q. Taking those boys present from the beginning of 1947 to the end of the investigation, both groups figured equally in the record. During the main period (2 and 3) and the control period (4) the agenised group appeared more frequently. More detailed analysis revealed, however, that the change in behaviour between the two groups took place before the change in diet. Further, many of these offences occurred in the main dining-room, and here the two groups appeared as psychologically significant ones.

TABLE III—DIETARY RECORDS

—	On agenised flour	On unagenised flour
Protein (g.)	81	76
Fat (g.)	101	99
Carbohydrate (g.)	338	310
Calories	2750	2610
Calcium (mg.)	929	856
Iron (mg.)	19	19
Vitamin A potency (I.U.)	8473	9237
Vitamin B (µg.)	1090	1018
Vitamin C (mg.)	50	50
Percentage of calories from flour products	46·1	43·8
Percentage of protein from flour products	51·0	48·2

Nov. 3–9, 1947, inclusive. Average intake daily of boys.

Dietary and Biological Controls

On four occasions during the test a careful analysis of dietary intake was made for each group. These analyses each covered a period of fourteen days. No constant differences were detected between the intake of the two groups, and the values were well above those accepted as the minimum requirements for children of this age-group. About 45% of the calories and about 50% of the total protein came from flour. Table III gives the results of a week's dietary survey. To check any possible error in the distribution of the two diets, samples of bread and flour from each batch were submitted for animal experiments. The untreated flour remained free from toxic action. The toxicity of the treated flour varied considerably but it generally caused severe symptoms in animals.

ADDITIONAL STUDIES

As the results of this survey were essentially negative, two adult volunteers undertook to live on a highly

* The material for these tests was kindly lent by the Air Ministry Training Research Division, from whom further details may be obtained.
† Kindly lent by the Department of Psychology, Cambridge University.

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agenised diet under constant medical supervision. A diet was devised in which the major part of both calorie and protein intake was derived from flour. All flour products were prepared from flour which had been treated with agene at the rate of 24 g. to the sack (9·6 g. per cwt.).

In addition to daily clinical observation, physiological and psychological investigations were repeated regularly. These included blood-count, erythrocyte-sedimentation rate, urinary and fæcal examinations, and blood-urea estimations on alternate days. At the end of the investigation tests of liver function were performed. Electro-encephalograms were recorded twice a week. None of these investigations revealed any change in physiological function.

The electro-encephalogram findings are of interest. The original record of one subject showed an abnormality (generalised outbursts of mixed frequencies, chiefly 6–10 cycles per sec.). This would have been consistent with a history of epilepsy, but no such history was obtained. During the consumption of agenised flour the abnormality persisted but showed no exaggeration. The electro-encephalogram of the other subject remained normal throughout.

During the investigation the subjects underwent psychomotor tests twice a week. Those used included triple tester, simple finger dexterity test, and Kohs blocks. No abnormality was detected in their approach to, or behaviour in, the test situation, and the scores obtained gave a typical learning curve.

In these two subjects no toxic effect was detected over a period of eight weeks.

SUMMARY AND CONCLUSIONS

The original intention of this investigation was to compare children from whose diet agenised flour had been excluded with children receiving flour agenised at the current commercial rate. After eight months no differences were detected.

Shortly before the investigation closed, supplies of flour agenised at 12 g. per sack became available. The effect of a diet prepared from this flour was tried on the children who had so far been free of agenised flour for eight months. Immediately after the change most of these children did not maintain their normal weight increase; but, on the other hand, their performance on the psychomotor tests was better. These changes do not reach a level of statistical significance, and their relation to the change in diet is not clear.

The children ate on the average 340 g. of flour a day. This represents about half their daily intake of calories, protein, and carbohydrate.

Two adult volunteers lived for eight weeks on a diet containing flour agenised at 24 g. to the sack, their average daily intake of the treated flour being 360 g. No impairment was noted in either physiological or psychological functions.

These results are in agreement with those obtained in America by Newell et al. (1947), who detected no changes in man. In their investigation five persons received 105 g. of wheat products a day for 14–28 days, with 3–20 g. of agene per cwt. of flour. They mention, however, that more detailed studies are shortly to be published.

Thus it is fair to conclude that the effects of commercially agenised flour on man is difficult to detect. It may be harmful, beneficial, or inactive.

This survey could not have been undertaken without the friendly coöperation of a large number of people. We wish especially to acknowledge the assistance of the headmaster, together with all his staff, the local authority, and the Ministries of Health and Food. We received technical assistance from, among others, Dr. Bruce White, at the National Institute for Medical Research, Mr. J. Done, of the Human Nutrition Research Unit, and Dr. J. N. Cumings, of the National Hospital. Dr. Margaret Ferguson kindly assisted with the psychological tests, and Dr. J. Billings, Dr. R. H. Fox, and Dr. Dean A. Smith with the clinical examinations. During part of the investigation Miss C. Searle S.R.N., assisted with the care and observation of the children. We are indebted to the continual interest and advice of Dr. E. A. Carmichael, Prof. B. S. Platt, and Dr. Eliot Slater. To Sir Edward Mellanby, who kindly arranged the animal controls, we are also indebted for considerable criticism and advice. Finally, without the willing coöperation and technical ingenuity of the millers such an extensive investigation would not have been possible.

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MORBIDITY AND FEEDING IN INFANCY

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SEVERAL years ago Dr. H. K. Waller suggested that the reason why the great superiority of the breast-fed child was not more widely recognised among doctors was that the doctors seldom saw any. Comparative morbidity-rates in breast-fed and bottle-fed infants have not been readily forthcoming, because they have been sought by workers in hospitals, whereas they should have been gathered by general practitioners.

Smellie [1] analysed a series of infants with enteritis. Of those who had been breast-fed for a month or more 25·9% died, whereas of those who had never been breast-fed 70·6% died.

Ebbs and Mulligan [2] showed that the proportion of children admitted to hospital were: breast-fed 15%, partially breast-fed 29%, and artificially fed 56%. These figures were in striking contrast with those derived from healthy children in the infant-welfare clinics of the same area, of whom only 29% were artificially fed.

Gairdner [3] investigated the early history of a series of babies admitted to hospital with enteritis. At the time of admission all were over a month old, and all were artificially fed. Of the 39 who had been breast-fed for a month or more 28% died, whereas of the 60 who had been breast-fed for less than a month 55% died.

The weakness of all these figures lies in the total subjected to analysis—a total which cannot be securely related to the general infant population of any area. Recently I have analysed 100 cases in my own practice to determine the number of domiciliary visits required for illness—other than notifiable diseases and accidents—during the first year of life. The number represents the total deliveries in the practice between certain dates. The following table analyses the data:

	No. of cases	*No. of visits*	*Average per child*	*No. not requiring any visit*
Breast-fed beyond 3 months	67	93	1·39	49 (73%)
Breast-fed beyond 1 month but under 3 months	12	53	4·42	3 (25%)
Artificially fed at or before 1 month	21	136	6·48	2 (9·5%)

I consider that these figures give a real indication of morbidity-rates, because they refer to an unselected series.

1. Smellie, J. M. *Lancet*, 1939, i, 969.
2. Ebbs, J. H., Mulligan, F. *Arch. Dis. Childh.* 1942, **17**, 217.
3. Gairdner, P. *Ibid*, 1945, **20**, 22.

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CLINICAL ESTIMATION OF BASAL METABOLIC RATE

THE RP INDEX

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THE main inconvenience of determining the basal metabolic rate (B.M.R.) by gas analysis lies in the necessity of keeping the patient strictly at rest and in the desirability of really accurate apparatus. Even under the best possible conditions normal readings fall within a wide range. Moreover, serial determinations to judge the efficacy of treatment are very time-consuming.

Several clinical methods requiring no apparatus have been described. The most useful of these, according to László and Horvátth (1941), are the Read II and Boothby methods. The Read II formula (Read 1922, 1924) is:

B.M.R. % (± normal) = 0·75 (pulse-rate + 0·74 pulse-pressure) − 72.

The Boothby formula is:

B.M.R. = pulse-rate × pulse-pressure.

The B.M.R. here is expressed as an index, the normal range being 2000–4000.

The methods based on gas analysis depend on the determination of the quantity of oxygen consumed during the period of observation. Patients with a B.M.R. above normal consume an abnormal quantity of oxygen. They also have a raised pulse-rate and respiration-rate. Conversely, in conditions with a low B.M.R. the pulse and respirations are usually slowed.

Kósa (1942) elaborated the following formula, which makes use of both pulse-rate and respiration-rate:

B.M.R. % (± normal) = 1·25 (pulse-rate + respiration-rate) − 116.

My experience with this formula (Bene 1943) in 100 consecutive patients led me to conclude that it did not correspond to the results obtained by the Krogh method. The error lies in the arithmetical structure of the formula, since patients with a B.M.R. raised above 15% (Krogh) did not show a corresponding increase by the Kósa formula. I have found, however, that by simply multiplying the pulse-rate by the respiration-rate an index is obtained which is a more reliable guide. This "RP-index" formula is:

B.M.R. = respiration-rate × pulse-rate.

The B.M.R. is expressed as an index—e.g., normal pulse-rate (72) × normal respiration-rate (18) = 1296. The normal range is 1100–1500; below 1100 the index indicates decreased, above 1500 increased B.M.R.

A series of 100 patients were investigated by the Krogh method, and at the same time the clinical data required to apply the Read II, the Boothby, the Kósa, and the RP-index formulæ were obtained. The table shows the degree of correspondence between these different methods and the Krogh method:

Krogh	No. of patients	Correspondence with Krogh (%) Read II	Kósa	Boothby	RP index
Above + 15%	43	23	33	33	67
Between +15% and − 10%	48	91	58	85	70
Below − 10%	9	60	100	40	70

The chief advantage of the RP index lies in its simplicity and its reasonable degree of correspondence to the Krogh method. It can usefully be applied during the clinical examination of a patient, and serial estimations can easily be carried out by this method in the treatment of hyper- and hypo-thyroidism.

To obtain the pulse-rate and respiration-rate the patient should lie quietly for five minutes before the investigation and should be unaware that his respiration-rate is being counted, for otherwise the rate will rise materially.

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Preliminary Communication

ACTION OF NORADRENALINE AND ADRENALINE ON HUMAN HEART-RATE

NORADRENALINE (arterenol) differs from adrenaline in having no methyl group; it must not be confused with its isopropyl derivative, 'Aleudrine.' Its pharmacology has been extensively studied (West 1947, 1948),[1] but for many years noradrenaline was thought to be only of academic interest since it had never been found in the body. More recently, however, von Euler[2] has demonstrated a noradrenaline-like substance in various normal tissues, and Holton[3] has extracted it from a human adrenal tumour. Noradrenaline may even transmit certain nerve impulses chemically.[4] It is therefore important that its actions on different organs should be carefully compared with those of adrenaline. An investigation into the effect of noradrenaline and adrenaline on the blood-flow in the limbs afforded an opportunity for us to compare their actions on the heart-rate and arterial blood-pressure, with interesting and unexpected results.

METHOD AND RESULTS

Normal men and women aged 20–45 were the subjects of the study. A saline drip was set up, with the needle in one of the antecubital veins, and the heart-rate and blood-pressure were noted every minute or so. After about 10 min. the saline was turned off and an infusion of noradrenaline or adrenaline was given (usually at the rate of 10–20 μg. per min.) for 3 min., during which the heart-rate and blood-pressure were recorded at ¼ min. intervals. After the infusion readings were continued, though less frequently, for about 10 min., and then the other drug was infused as above. In some

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2. von Euler, U. S. *Acta physiol. scand.* 1946, **12**, 73.
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4. Bacq, Z. M. *Arch. int. Physiol.* 1933, **36**, 167. Gaddum, J. H., Goodwin, L. G. *J. Physiol.* 1947, **105**, 357.

ACTIONS OF ADRENALINE AND NORADRENALINE ON HEART-RATE

Subject	Rate of infusion (μg./min.)	Maximal change in heart-rate per min. during 3 min. infusion: Adrenaline	Noradrenaline
1	5	+45	+7
	15	+42	−12
2	10	..	±6
	20	+28	..
3	10	+40	−12
	10	+12	..
	20	..	−12
	20	+33	−12
4	10	+30	−12
	10	+40	..
	20	..	−24
	20	+45	−21
5	30	+30	−18
6	10	+35	−10
	10	+18	−16
	20	+46	−12
	20	+21	−27
7	10	+27	−6
	10	+12	−18
	20	+36	−9
	20	+13	−13

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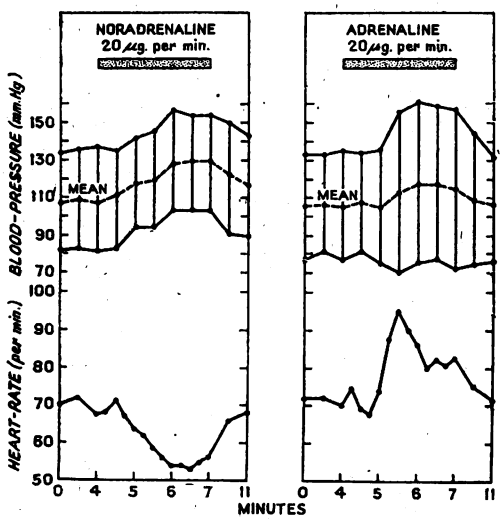
experiments the noradrenaline was given before and in some after the adrenaline.

In the body noradrenaline is present as *lævo*-noradrenaline,[5] and the lævo form was used in these experiments. The adrenaline solutions were made from 1 ml. ampoules of 1 : 1000 *l*-adrenaline hydrochloride (B.D.H.).

The table shows the remarkable difference in the actions of adrenaline and of noradrenaline on the heart-rate, adrenaline causing tachycardia and noradrenaline bradycardia. This is also seen in the figure, which shows the averaged results of all the 20 μg. per min. doses of adrenaline and of noradrenaline on the heart-rate and on the arterial blood-pressure. The partial subsidence of the adrenaline tachycardia during the course of the infusion was noted by Allen, Barcroft, and Edholm.[6] Subjective effects during the adrenaline infusions included



Arterial blood-pressure and heart-rate before, during, and after intravenous infusion of noradrenaline and of adrenaline; averaged results.

mild palpitation, hyperventilation, tightness in the chest, and muscular fatigue. There were usually no subjective sensations during infusions of noradrenaline.

DISCUSSION

The explanation of the different action of adrenaline and of noradrenaline on the heart-rate is not known. Two factors are probably concerned—the direct excitatory action of the drug on the pacemaker; and its reflex inhibitory action due to its pressor action on the vascular system.

SUMMARY

Noradrenaline, which differs from adrenaline in having no methyl group, has been found in various tissues including an adrenal tumour. It may be a chemical transmitter of sympathetic nerve impulses.

The actions of intravenous infusions of noradrenaline and of adrenaline on the heart-rate and arterial blood-pressure have been observed.

In doses of 10–20 μg. per min. noradrenaline causes bradycardia whereas adrenaline causes tachycardia.

We are grateful to Dr. H. J. Swan, research fellow of St. Thomas's Hospital, for valuable assistance. We also thank the subjects for their coöperation, and the Sterling-Winthrop Research Institute for a supply of *l*-noradrenaline to H. K.

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Medical Societies

ROYAL SOCIETY OF MEDICINE

Streptomycin in Tuberculous Meningitis

THE neurological section of the Royal Society of Medicine, with Dr. WILLIAM JOHNSON, the president, in the chair, on Jan. 6 held a symposium on the streptomycin treatment of tuberculous meningitis.

Sir HUGH CAIRNS and Dr. MARGARET TAYLOR reported on 49 cases (47 were proved bacteriologically) treated with this drug at the Radcliffe Infirmary and Military Hospital for Head Injuries. Of these, 20 had died—14 within three months of the commencement of treatment, 4 within six months, and 2 thereafter.

One example of successful treatment was a youth who was ill in bed for 8 months, in hospital for a further 6 months, and returned to work 2 months later. Streptomycin had been continued for 8 months, with 101 days' intrathecal administration. Cultures of the cerebrospinal fluid (C.S.F.) were positive sporadically up to the 27th day of treatment, and an attack of acute arterial hypertension developed on the 70th day. The cell-count and protein in the C.S.F. did not return to normal until 20 months. This patient had been back to work for 7 months, and the only residuum of his illness was complete amnesia for the first 4 months in hospital and the 5 months before his admission.

Sir Hugh Cairns emphasised the chronicity of the condition, and indicated the necessity for prolonged treatment. Their cases had received streptomycin by the intramuscular route for 6 months or more and intrathecally for 6 to 12 weeks. In this respect they differed from the practice at some other centres where various intrathecal courses were interspersed with rest periods; but he felt that each centre should persevere with one particular type of treatment in order to give it a fair trial. Any regression in the clinical condition, or late positive films or cultures, called for prolongation of intrathecal treatment. When the acute phase was past, the possibility of surgical measures should be considered with a view to eliminating other foci of tuberculous infection. As with tuberculosis elsewhere in the body, the tuberculous process in the meninges called for lengthy observation after treatment was completed.

Some hydrocephalus developed in all the cases, and in many was proved by air encephalograms. In only 2 could this be attributed to complete obstruction by the basal exudate; the remainder had "replacement" hydrocephalus. For ventricular therapy burr-holes were made as a routine. These could then be used for continuing treatment if spinal block developed, or to rest the lumbar region in prolonged intrathecal courses; he regarded this route as less dangerous than the cisternal.

Regarding the general prognosis, their figures showed that patients with miliary or adult type of pulmonary tuberculosis did much worse than those relatively simple cases where a previous active lesion had been overcome. From a survey of published results he thought that the recovery-rate lay somewhere between 10% and 50% in different centres, and that with experience these figures would be improved upon. Results in the treatment of children under seven years of age were entirely comparable with those in other age-groups. He ended with a plea that the more general availability of streptomycin should not cause cases to be deflected from the centres which already have considerable experience of this work until the best methods of treatment have been decided.

Dr. P. M. DANIEL, discussing the morbid anatomy, said that one of the changes seen as a result of streptomycin treatment was a tendency for the conversion of the gelatinous exudate into one of woody hardness. This was due to the chronicity of the disease and not to streptomycin. This exudate caused interference with the C.S.F. circulation and affected the arterial system. Much had been written about the basal exudate and not enough about its extensions throughout the subarachnoid space. The arterial changes often led to infarction of the basal ganglia and the mid-brain, among other areas. Transient dementias might be attributable to an encepha-

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litis. Active foci in the depths of the sulci, he suggested, might well be the source of reinfection and relapse.

Dr. I. DONIACH confirmed from the histologist's viewpoint that nothing new had emerged as the result of streptomycin treatment. The changes in the histological appearances were due to prolongation of the life of those with the disease; in sections from untreated cases of meningitis he was able to demonstrate all stages of arteritis to the complete obliteration of the lumen which is seen after long streptomycin treatment.

Dr. I. A. B. CATHIE pointed out that rapid return to normal of the C.S.F. constituents was often seen after far shorter periods of treatment than those named by Sir Hugh Cairns. Chlorides in the C.S.F. were an unreliable guide: the behaviour of the C.S.F. sugar content was probably the most reliable diagnostic and prognostic index. He drew attention to the possibility of using adjuvant measures of therapy; he himself had been trying, with promising results, a fibrin-solvent prepared from streptococci.

International Tensions

At a joint meeting of the psychiatry section with the British Psychological Society on Jan. 11, with Dr. J. R. REES in the chair, a discussion was held on the tensions affecting international understanding.

Dr. OTTO KLINEBERG, who directs the division of UNESCO's department of social sciences which is working in this field, said that research was proceeding along five principal lines: (1) the distinctive character of the various national cultures, knowledge of which might be a major factor in international understanding; (2) the notions that one nation had about another (the so-called stereotypes); (3) methods of attitude change (for example, the relation of prejudice in teachers to prejudice in children); (4) influences predisposing to international understanding on the one hand and to aggressive nationalism on the other; and (5) the relation of intranational tensions, and particularly of minority problems, to international relations.

Understanding, he said, might be intellectual (in the sense of knowledge) or emotional (denoting friendliness); and though possibly unrelated, both were relevant. Tension he defined as a state of strain, tending to give rise to action which was often hostile or aggressive. Were personal tensions responsible for international tensions? He made no such assumption. Nevertheless, the individual's mental health and his attitude to the outside world were related, and there was a significant positive association between personal tensions (particularly with a sense of insecurity) and hostility to "foreigners." Moreover, there tended to be a generality of hostility; the man who expressed animosity against one nation usually felt the same way about others.

In whose minds did war begin? So far the work had been concerned with the masses rather than with leaders, but the attitude of the masses was relevant to leadership. As a psychologist, he confessed that the research had hitherto shown a bias towards psychological investigation; historical, economic, and political factors must also be studied. What was being done about the real tensions? The difficulties here were great; and he had failed to get together experts from every nation. "Every time we come across a real tension we are told that it is too hot to handle." However, his division had been asked to study the relationship of India and Pakistan.

The project had value as a central rallying-point for social scientists, psychologists, psychiatrists, and others. Only when enough information had been collected would this be passed on to educationists.

Dr. JOHN RICKMAN complained that group tensions had hitherto been studied mostly from without; research-workers who went into the group with their own questions were liable to miss the mark, for the character of tensions had to be discovered from within. To his knowledge, each of two groups of experts studying international tension had refused first to submit to analysis of their own tensions; and it was hardly surprising that other investigators had been told that current international tensions were "too hot to handle." Possibly the first object of group studies should be to investigate resistance to examination within the group. "Is the study of tensions within the group more distressing than war?"

Prof. T. H. MARSHALL pointed out that UNESCO is an international body. The research project called for coöperation and objectivity, so certain issues were ruled out; the workers engaged in it could not report on matters sub judice. He expressed particular interest in the compulsive influences which seemed to lead men in key positions to do something which they apparently did not want to do.

Dr. H. V. DICKS pointed to the worth of the project in research, training, and therapy. International tensions, though on a large scale, did not involve, in his view, any new concepts.

Mr. E. A. SHILS complained that psychologists tended to explain great events from a single impulse—aggressiveness. There was woeful unpreparedness for analysing élite behaviour.

Dr. ERNEST JONES suggested that the project did not come close enough to grip with the major problem. It had a mild name: what was really under review was enmity or hostility, including hostility of the individual to himself. It was popularly held that international troubles started through fear; but fear did not start of itself—it always had an object. History showed that aggressiveness was greater on one side than the other. In the last 2000 years waves of aggressiveness and expansion had touched most of the great nations and then passed on. What tensions had arisen to cause these waves? The historian should lay the facts before the psychologist, in an attempt to discover any helpful generalisation.

Reviews of Books

Viral and Rickettsial Infections of Man

A Symposium. Editor: THOMAS M. RIVERS, M.D., Rockefeller Institute for Medical Research. Philadelphia and London: J. B. Lippincott. 1948. Pp. 587. 45*s*.

KNOWLEDGE of the viruses and rickettsiæ has recently grown so fast that it has been difficult for any author to produce a book that would not be out of date before it appeared on the bookstands. Moreover, until recently, controversy has reigned over many of the fundamental properties of viruses. Dr. Rivers and his 26 American associates think that knowledge has now become sufficiently stable, and opinions sufficiently harmonious, to justify the symposium they offer us. Many of them have themselves added to knowledge of their subjects: for example, M. Theiler writes on yellow fever, H. A. Howe on poliomyelitis, W. M. Stanley on the chemical and physical properties of viruses, and K. F. Maxcy on epidemiology. The brief general introduction, by Rivers, could with advantage have been enlarged. The book has enough emphasis on the clinical aspect, diagnosis, and treatment to justify the claim that it is written for students and practising physicians; and it is remarkably readable. But it is not so much a simple review as a comprehensive work. Indeed its value may be greater to those engaged in actual work on viruses, since they will have the background essential for perspective.

To those with less special knowledge, F. L. Horsfall's three chapters on the common cold, primary atypical pneumonia, and influenza may convey a somewhat false impression of our understanding of virus diseases of the respiratory tract as a whole; for though the chapter on influenza is a model, particularly in setting out the properties of the influenza viruses, the absence of any account of the unsolved problem of acute respiratory disease not due to these viruses suggests an omniscience we do not possess. The reader may conclude that all that is neither influenza nor the common cold must be primary atypical pneumonia; but the multitude of viruses claimed to be the causal agent of this syndrome may well depress rather than enlighten him. The list of animals pressed into use in the investigation of primary atypical pneumonia includes twenty species, but the striking success of influenza and the ferret has not been repeated.

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Separate chapters deal with the typhus fevers (epidemic and murine), the spotted-fever group, including the newly described rickettsial pox, scrub-typhus, and Q fever. Snyder's chapter on typhus is a balanced account of disease and causative agent, with proper emphasis on history and on control measures; chloromycetin had apparently not reached the stop-press in time for typhus fever but it figures in the account of scrub-typhus.

By any standards this book is lavishly produced, and its moderate price is due to assistance from the American National Foundation for Infantile Paralysis.

Vision and the Eye

M. H. PIRENNE, DR.SC. Liége, PH.D. Camb., Imperial Chemical Industries research fellow, University of London. London: Pilot Press. 1948. Pp. 187. 12*s*. 6*d*.

Dr. Pirenne writes about the physiology and physiological optics of the eye from the standpoint of the scientist rather than of the clinician. His book is intended for the non-specialist reader, though it demands some knowledge of physics, chemistry, and mathematics. Subjects covered include the formation of the retinal image, the structure and function of the retina, colour-vision, the nervous activity produced in the eye, and the eyes and vision of insects. For doctors, at any rate, the information would have been more interesting if it had been linked to clinical signs and symptoms; a description of such phenomena as fatigue, adaptation, and accommodation with relation to the sight would have been welcome. Nevertheless, this is a useful work and puts in an attractive and straightforward manner the facts behind the function of vision.

Diagnostics pratiques

NOEL FIESSINGER and 19 collaborators. Paris: Masson. 1948. Pp. 656. Fr. 1200.

As Prof. A. Lemaire says in his preface, this book is the last message from Noel Fiessinger, so long a clinician at the Hôtel-Dieu in Paris. It is conceived on an ample scale, and achieves a uniformity remarkable in the combined work of some twenty authors. To the English reader it offers a valuable survey of French medicine, and the somewhat novel method of presentation will appeal to him. Of the eleven large chapters each is subdivided into major symptoms or signs; thus the second chapter, on general processes, deals with fatigue, wasting, obesity, glycosuria, œdema, and prolonged and periodic fever. For each subject there are three headings —Les Reconnaître, Les Distinguer, and Les Expliquer. It is from such diagnosticians as Fiessinger that the beginner in medicine learns that diagnostic errors are less often due to ignorance than to lack of care in examination, and lack of thought, time, and common sense. The book does not touch on laboratory or radiological examinations, but it is a thoroughly practical textbook of bedside medicine, so well presented that one is hardly conscious of the absence of illustrations. It will be a lasting memorial to its senior author.

Sterility and Impaired Fertility

(2nd ed.) C. LANE-ROBERTS, C.V.O., M.S., F.R.C.S., F.R.C.O.G.; ALBERT SHARMAN, M.D., M.R.C.O.G.; KENNETH WALKER, M.B., F.R.C.S.; B. P. WIESNER, D.SC.; MARY BARTON, M.B. London: Hamish Hamilton Medical Books. 1948. Pp. 400. 24*s*.

NEARLY ten years have elapsed since the publication of the first edition of this useful book. It is perhaps depressing to reflect how little the past decade has added to our positive knowledge of, or power to treat, sterility in either sex.

The general arrangement of the book has not been materially altered but the contents have been revised. After a general survey, the next five chapters are devoted to male infertility, clinical examination, coital technique, the characteristics of semen (including methods of collection, examination, and evaluation), the physiology and pathology of the male reproductive mechanism, and treatment. More emphasis than hitherto is laid on the importance of dealing with infections, both local and remote; the gonadotrophins are still recommended (though in somewhat larger doses) in the treatment of azoospermia and lesser degrees of deficient spermatogenesis, though their value, judging by a short series of cases quoted, remains uncertain. In the second half of the book, infertility factors in women, the treatment of female infertility, and artificial insemination both with husband's and donor's semen, are discussed. The section on the cervical factor and the assessment of its normality or otherwise by means of post-coital tests and invasion tests in vitro has been brought well up to date. There are a few surprising omissions: no mention is made of Mann's work on fructose in semen, nor of the administration of progesterone by means of implant.

Several new and valuable appendices have been added, notably those on the technique of the Sims and invasion tests, basal temperature charts, and X-ray and diathermy therapy.

Lehrbuch der Augenheilkunde

Editors: M. AMSLER, Zürich; A. BRÜCKNER, Basle; A. FRANCESCHETTI, Geneva; H. GOLDMANN, Berne; E. B. STREIFF, Lausanne. Basle: S. Karger. 1948. Pp. 858. Sw. fr. 85.

THIS book arose out of the Swiss need for textbooks during the war, when works from abroad were not to be had. The five editors held the five chairs of ophthalmology in Switzerland, and they have had the assistance of twelve Swiss colleagues and of Prof. H. Weve of Utrecht. It follows fairly closely the usual treatment of ophthalmology in textbooks, except that it has an extensive introductory section dealing, among other things, with general symptomatology, heredity, social aspects, and therapeutic principles, and a concluding section on general aspects of ophthalmology. As might be expected from the panel of contributors, the teaching is both orthodox and authoritative; but it shows local colour, particularly in methods of treatment, and has a welcome freshness of outlook. As a student's book it could hardly be better.

Nuts (London: Faber. 1948. Pp. 264. 18*s*.).—This book, by Mr. F. N. Howes, D.SC., principal scientific officer at Kew, is extremely useful for reference, and will be a godsend to vegetarians whose diet is naturally somewhat lacking in concentrated foodstuffs. It is well written, authoritative, and well produced. It should call further attention to a much neglected source of food.

A Practical Manual of Diseases of the Chest (3rd ed. London: Oxford University Press, 1948. Pp. 670. 50*s*.). —Dr. Maurice Davidson has brought this manual up to date by drastic revision of the sections on the pathogenesis of bronchiectasis, the chemotherapy of lung inflammation, silicosis, and extrathoracic new growths. Recent advances in tuberculosis of the lung have also been included. Two fresh chapters on cysts of the lung and pleura and on sarcoidosis have been added. There is a considerable number of new illustrations, which are of a high standard of excellence. This well-balanced and readable account of the subject has now become a standard work for practitioners and senior students.

Emergency Surgery (6th ed. Parts I and II. Bristol: J. Wright. 1948. Pp. 388. 21*s*. each part).—During the eighteen years since the first edition of this book was published many young surgeons have been indebted to Mr. Hamilton Bailey for his clear and practical advice in the problems of emergency surgery. Their successors will welcome this new edition, and others more senior will perhaps be glad to refresh their memory about conditions which they rarely encounter. The two parts so far published deal with some general matters, including infusion, transfusion, and anæsthesia, and with the abdomen. Mr. Bailey's technique is effective: he is concise but sufficiently detailed to give the inexperienced surgeon all the guidance he can get from a book—and that is nearly as much as he needs. The advice is definite, but alternative methods of treatment are not entirely neglected. Illustrations are plentiful and strictly relevant, while sample case-histories, succinctly reported, bring the general text sharply into focus. The accent throughout is on treatment; and comparatively little is said about diagnosis, though its importance is stressed in several places. This is a defect, but it may be that to deal adequately with diagnosis would have doubled the size of the book, and to deal with it inadequately would have been worse than useless. The issue of the book as a serial in five parts is tiresome for the reader, who will probably not be consoled by the reasons given in the preface.

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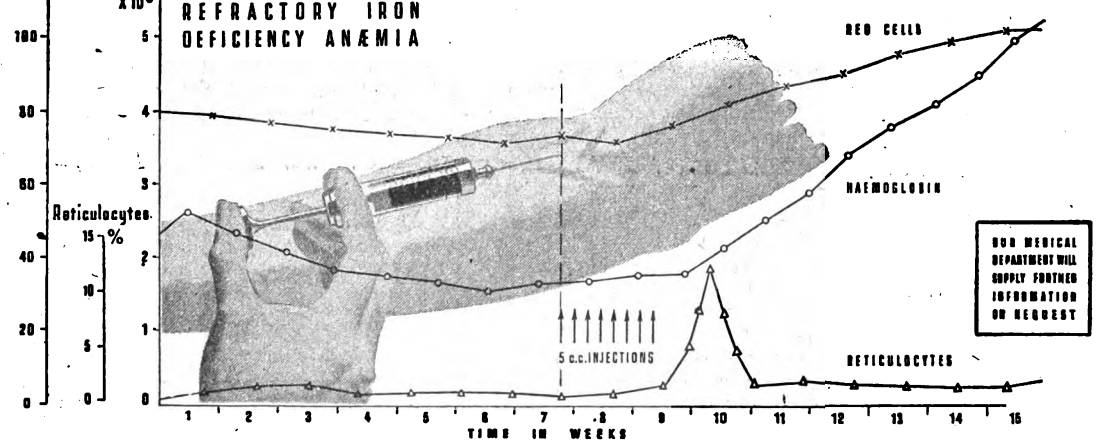

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References:—Shortage of space precludes list of references, but full documentation may be obtained on application to Medical Dept. 41.B.

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References:—Full documentation may be obtained on application to Medical Dept. 50.A.

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THE LANCET

LONDON: SATURDAY, JAN. 22, 1949

Substitutes for Plasma

APART from the introduction of gum-acacia by W. M. BAYLISS during the first world war, little effort was made until the second world war to prepare artificial fluids that could be infused to restore the volume of the circulating blood. In the '20s and '30s whole blood was used for this purpose in slowly increasing quantities, and in the middle '30s human plasma and serum were employed in Russia and America for the treatment of "shock"; but it was not until 1939 that the demand for blood and plasma became so great that the question of substitutes was reopened. Today in Great Britain we have the transfusion services developed during the war, and the provision of plasma is part of their work. So long as blood-banks remain a feature of hospitals, there will always be time-expired blood to use as a source of plasma; and the risk of plasma transmitting homologous serum jaundice can probably be overcome by its irradiation with ultraviolet light.[1] Yet, even so, there are occasions in this country in peace-time when a substitute for plasma would be useful, and it would have great value abroad wherever plasma is unobtainable or is liable to deteriorate. Its possible importance in time of war is obvious.

Most of the substances proposed and tested have failed to meet one or more of the theoretical requirements of a plasma substitute set out by Dr. BULL and his colleagues in our present issue. Gum-acacia was suspect before the late war. Of the many other substances investigated—pectin, gelatin, bovine albumin, bovine plasma and serum, isinglass, methyl cellulose, polyvinylpyrolidon, polyvinyl alcohol, ascitic fluid, and the glucose polymer dextran—all seem to have disadvantages, except perhaps the last, which is now receiving closer attention. Though its possibilities were considered in England early in the war, the credit for producing dextran in a form suitable for infusion belongs to the Swedish workers GRÖNWALL and INGELMAN,[2] BOHMANSSON et al.,[3] and Dr. THORSÉN whose latest paper we publish this week. Dextran is now freely used in Sweden, where there is no nation-wide transfusion service, and, judging by published reports, experience has been uniformly favourable. Corroboration is now provided by the results of a laboratory and clinical trial of British-made dextran, by Dr. BULL and his colleagues, showing that it is a bland, non-toxic, non-antigenic fluid which, in cases of burns and in subjects suffering from "shock" or hæmorrhage, appears to be as beneficial as plasma. It seems to fulfil the theoretical requirements with the single exception that its disappearance from the body is probably slow. Whether it is completely metabolised as glucose, or whether it is broken down to a lower molecular weight and slowly excreted, remains to be seen. GOLDENBERG et al.[4] have reported histological changes in the kidneys—apparently temporary—after its use, but they do not clearly define the type of dextran they infused; and introduction of dextran into animals in quantities larger than any likely to be given to human beings has caused no such changes. Dextran molecules smaller than 70,000 are excreted within a comparatively short time, and it is possible that, where renal function was already depressed, the added excretory load thus imposed might be dangerous. This possible drawback might well be overcome if dextran could be prepared, as Dr. BULL and his colleagues suggest, without the small molecular fraction.

One of the great merits of dextran is that it can probably be manufactured to conform closely to the ideal specification of an artificial substitute for plasma. We hope, therefore, that the more extensive trial proposed by the British workers will be carried out, so that the fate of dextran in the body, and any remote harm it can do, may be fully revealed. Its keeping qualities under tropical and other climatic conditions also need investigation.

1. Blanchard, M. C., Stokes, J., Hampil, B., Wade, G. R., Spizizen, J. *J. Amer. med. Ass.* 1948, **138**, 341.
2. Grönwall, A., Ingelman, B. *Acta physiol. scand.* 1944, **7**, 97; *Ibid*, 1945, **9**, 1; *Nature, Lond.* 1945, **155**, 45.
3. Bohmansson, G., Rosenqvist, H., Thorsén, G., Wilander, O. *Acta. chir. scand.* 1946, **94**, 149.

Vitamin B_{12}

IT is now about nine months since LESTER SMITH in England, and RICKES and co-workers in the U.S.A., described the preparation from liver of crystalline anti-anæmic materials which were active in much smaller doses than any that had been tried before.[5] The Americans gave their crystals the non-committal name "vitamin B_{12}," and LESTER SMITH's material seemed to be a less purified preparation of the same substance. RICKES et al. have since stated that this anti-anæmic material is a "cobalt coördination complex,"[6] and LESTER SMITH[7] reports that the molecule has a weight of about 1500 and contains 4% of cobalt. Nevertheless, such evidence as there is suggests that cobalt by itself has no anti-anæmic activity in pernicious and similar anæmias. Vitamin B_{12} is present only in minute amounts in liver—a ton of fresh liver yields 250 mg. or so. But it is also active in minute doses; given parenterally to a patient with pernicious anæmia in relapse, a few microgrammes suffice to produce a reticulocyte response and start the marrow on its change from megaloblastic to normoblastic erythropoiesis.

Since the original announcement, results with vitamin B_{12} have been reported in various diseases. So far as is known it acts only on the anæmias characterised by a megaloblastic change in the bone-marrow—i.e., pernicious anæmia, nutritional megaloblastic anæmia, sprue, and a few other rare diseases. The material is scarce, so reports are few, but they are consistent. SPIES and co-workers[8] gave single doses

4. Goldenberg, M., Crane, R. D., Popper, H. *Amer. J. clin. Path.* 1947, **17**, 939.
5. See leading article, *Lancet*, 1948, **i**, 715.
6. Rickes, E. L., Brink, N. G., Koniuszy, F. R., Wood, T. R., Folkers, K. *Science*, 1948, **108**, 134.
7. Smith, E. L. *Nature, Lond.* 1948, **162**, 144.
8. Spies, T. D., Stone, R. E., Aramburu, T. *Sth. med. J.* 1948, **41**, 522.

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of 6–15 μg. to patients with pernicious anæmia, nutritional macrocytic anæmia, and non-tropical sprue. The responses were definite but minimal; there was a reticulocytosis and there was normoblastic transformation in the marrow, but the rise in red cells and hæmoglobin was not significant. In 5 Cuban patients with tropical sprue who were given doses of 10–25 μg. there was a good initial response, but the patients soon relapsed; SPIES therefore thinks that 100 μg. is the minimum dose for producing remission, and he notes that 400 g. of whole liver by mouth, presumably containing about 100 μg. of B_{12}, was highly effective.[9] He and his colleagues[10] treated successive relapses in cases of pernicious anæmia, nutritional macrocytic anæmia, and tropical sprue with thymine, folic acid, and finally B_{12}. They found that the effective maintenance dose of thymine was 6–10 *grammes* daily and of folic acid 10 *milligrammes* daily, whereas B_{12} produced a reticulocytosis in doses of 6–23 *microgrammes* though the subsequent rise in red cells and hæmoglobin was poor. PATEL[11] gave larger doses—80 μg.—of LESTER SMITH's crystals to 2 patients with Indian sprue, but they only responded like those whom SPIES had treated with much smaller doses of B_{12}. Too few cases have so far been followed to give an idea of what the maintenance dose of B_{12} will be. In the case of pernicious anæmia described by BERK et al.,[12] before treatment the patient's blood had 1,920,000 red cells per c.mm. and 6·5 g. of hæmoglobin per 100 ml.; she received 55 μg. of B_{12} parenterally over 24 days, 40 μg. being given in the first 8 days, and her red-cell count rose to 3,380,000 per c.mm. with 10·2 g. of hæmoglobin per 100 ml. Thus rather more than 2 μg. daily produced a relatively poor response compared with that seen after the use of a potent liver extract; but it seems clear that if a dose of 5 or 10 μg. daily had been practicable a comparable response would have been obtained. At the Mayo Clinic, HALL and CAMPBELL[13] have treated 11 cases of pernicious anæmia in relapse with B_{12} and have followed them for one to five months. In 2 patients 1 μg. daily produced an optimal hæmatopoietic response, and satisfactory responses were obtained in 3 patients given 25 μg. once a week and in a fourth who received 5 μg. daily for five days and then 5 μg. thrice weekly. These workers agree with others that 1μg. of B_{12} is about equivalent to 1 *U.S.P.* unit of liver extract.

BERK and his co-workers were mainly concerned with the effect of B_{12} on their patient's neurological symptoms. This is an important matter, since the failure of folic acid to influence the combined degeneration of the cord is one of the main reasons why folic acid cannot be the anti-anæmic principle of liver and is unsuitable for the routine treatment of pernicious anæmia. If vitamin B_{12} is in fact the anti-anæmic liver principle, it must be shown to relieve the spinal-cord symptoms as well as the anæmia. The patient treated by BERK and others had definite signs of tract involvement—extensor plantar responses and sensory defects—and when B_{12} was given, and the anæmia remitted, these signs, together with the paræsthesia present, disappeared. Of the 11 cases reported by HALL and CAMPBELL, 6 had peripheral neuritis plus early or advanced combined degeneration, and in 5 of these the neurological manifestations improved satisfactorily during the few months' observation. In 3 cases the improvement is described as remarkably rapid. These results are encouraging but do not, of course, suggest that B_{12} has any special place in the treatment of subacute combined degeneration; similar results could have been obtained with a potent liver extract. There is evidence that commercial liver extracts contain vitamin B_{12}, and at the recent London Medical Exhibition one firm showed red crystals, like those of LESTER SMITH, obtained from their particular brand. This is interesting when we remember that the folic acid in commercial liver extracts was found to be very variable and even undetectable. If vitamin B_{12} is the anti-anæmic principle, then all potent liver extracts must contain it; but we know that liver extracts, particularly the more purified types, have at best only a partial effect on the organic signs and symptoms of those patients with subacute combined degeneration who have no significant anæmia; so the demonstration of B_{12} in these extracts damps our hopes—based admittedly on very tenuous evidence—that it will relieve these chronic sufferers.

Another consequence of the discovery of vitamin B_{12} will certainly be developed. The American workers checked their progress by the ability of their extracts to support the growth of *Lactobacillus lactis* Dorner. If commercial liver extracts owe their anti-anæmic activity to vitamin B_{12} it might be possible to assess their potency by a similar microbiological test. Investigation of this subject will call for a joint effort by those who can carry out the difficult microbiological technique and physicians who see untreated pernicious anæmia patients and are familiar with the pitfalls of clinical testing; a large number of parallel tests will be needed, using several extracts, and suitable patients are not found in large numbers in any one clinic. The technique of microbiological assay has also been used to search for other possible sources of vitamin B_{12}. RICKES and his team[14] have now isolated from broth cultures of *Streptomyces griseus* a red crystalline material with all the properties of vitamin B_{12}, including the presence of cobalt and phosphorus and ability to produce a clinical response in pernicious anæmia. It may be said that when we know the chemical constitution of vitamin B_{12}, whether it can be synthesised and prepared at an economic price (perhaps from some source other than liver), and whether it really reproduces all the properties of potent liver extracts, then neither microbiological assay nor clinical testing will be needed. But though all these points are being tackled they are unlikely to be solved very quickly or very easily. Meanwhile the practitioner will be well advised to keep to the recognised methods of treatment—with liver extracts that have been clinically tested before issue, or, if treatment by mouth is preferred, with desiccated stomach.

9. Spies, T. D., Suarez, R. M. *Blood*, 1948, **3**, 1213.
10. Spies, T. D., Stone, R. E., Lopez, G. G., Milanes, F., Toca, R. L., Aramburu, T. *Lancet*, 1948, ii, 519.
11. Patel, J. C. *Brit. med. J.* 1948, ii, 934.
12. Berk, L., Denny-Brown, D., Finland, M., Castle, W. B. *New Engl. J. Med.* 1948, **239**, 328.
13. Hall, B. E., Campbell, D. C. *Proc. Mayo Clin.* 1948, **23**, 584, 591.
14. Rickes, E. L., Brink, N. G., Koniuszy, F. R., Wood, T. R., Folkers, K. *Science*, 1948, **108**, 634.

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Venereal Diseases

THE late CHARLES GIBBS, of Charing Cross Hospital, used to teach that future generations would refer to ours as the syphilitic age; adding cheerfully, however, that the end was in sight; for, though modern methods of treatment might not always cure outright, they quickly made the patient non-infective. Mr. GIBBS would have had better grounds for his optimism today, when we have penicillin as well as arsenic and bismuth. But the tendency towards improvement was interrupted by the war; and even after it, in 1946, the return from overseas of many infected young men led to a spectacular increase of new cases of syphilis attending centres for the first time.[1] The numbers rose, indeed, from 5214 men and 5527 women in 1945 to 10,705 men and 6970 women in 1946. Moreover, spread is always favoured by the fact that the signs of early syphilis are usually noted later in women than in men, and a promiscuous woman can unwittingly spread infection for longer than a promiscuous man. Women likewise play the chief part in spreading gonorrhœa; for which, in 1946, 36,912 men and 10,431 women attended treatment clinics. This emphasises the importance of tracing contacts—a process which cannot yet be called really successful in this country, for of 3441 women and 271 men notified as contacts in 1946 less than half the women and only just over half the men were examined. Defence regulation 33B—which made it an offence for any person to refuse medical examination and treatment if he or she was declared by two or more patients to be the source of infection—was then in force, and 136 of the women and 3 of the men were compulsorily examined under it; but this regulation expired thirteen months ago.

These figures show that protection of healthy people from infection with venereal disease is still far from adequate; and it may be worth examining current American methods of propaganda which are said to be highly effective. For example, between November, 1947, and May, 1948, the *Columbus Star*, a weekly journal circulating in Ohio, published 23 venereal-disease case-histories, each accompanied by a statement from the doctor in charge of the Central Ohio rapid treatment centre.[2] This series caused many people to seek treatment early and is said to have been favourably received by all but a very small proportion of the public. The journal also offered to send free educational material, obtained from the United States Public Health Service, to any who wrote for it, and the response was immediate and great. "No squeamishness or false modesty was seen in the requests": housewives asked for copies for young people; clergy asked for material for group reading to parishioners; booklets for "teen-agers" were in demand; trade unions, industrial nurses, servicemen, the head of a police moral squad, college students, boys' clubs, and high-school hygiene classes all sought this information. The inference seems to be that people, at any rate in Ohio, are ready to learn and are not easily shocked. American campaigns have gone further perhaps than we should be inclined to follow them: we should not like to have loudspeakers in the streets which alternated venereal-disease messages with boogie-woogie rhythms. But there is surely a good case for intensifying the instructive efforts of our Ministry of Health, and for broadcasting more information on the lines of the impressive radio talk that Sir WILSON JAMESON gave in 1942.

Public education is perhaps the predominant need in any campaign for controlling venereal disease, and is essential for efficient case-finding; but the second great need is to hold the cases during treatment. It is noteworthy that the patients in Ohio were urged to attend the *rapid* treatment centre. The psychological effect of this name must have been great; and surely the adjective could nowadays be fairly applied to all treatment centres. For even though, in the treatment of syphilis, a course of bismuth and arsenicals is required to supplement penicillin, the time taken to achieve clinical cure is much shorter than formerly; and for gonorrhœa it is short by any reckoning. Case-holding remains as important as ever; for even penicillin is not a magic potion, and relapses are not so rare that they can be disregarded. Efficient case-finding and case-holding, and public instruction, were two of the nine requirements for venereal-disease control laid down ten years ago by THOMAS PARRAN, then surgeon-general of the U.S. Public Health Service. The others were provision of a trained public-health staff to deal with syphilis in each State and city; premarital and prenatal serodiagnostic tests; proper diagnostic services; sufficient treatment facilities; proper distribution of antisyphilitic drugs; routine serodiagnostic tests; and a scientific information programme. Before he retired, PARRAN saw most of those nine requirements fulfilled in the larger centres of population in his own country. Venereal-diseases control officers, contact-tracing organisations, and venereal-diseases central files are to be found in most of the public-health departments of the big cities, and about $2^1/_2$ million premarital or prenatal blood examinations are made each year in the 36 States or Territories where such tests are obligatory. Some 3000 clinics and 63 rapid treatment centres have now been established, and the number of serum tests performed has increased in ten years from $2^1/_2$ million to about 20 million. Venereological information is given to practitioners at regular seminars and conferences held at intervals up and down the States, and the U.S. Public Health Service sponsors the *Journal of Venereal Disease Information* which is freely distributed to those interested. The results of all this cannot be easily judged, for the incidence and mortality of venereal diseases, as of other infections, are governed by a great many factors—both medical and social—and the same sort of epidemiological trends have lately been apparent in various countries involved in the war. Nevertheless, the advocates of active endeavour can claim some support for their efforts from the facts that the death-rate from syphilis in the U.S.A. declined from 16 per 100,000 in 1937 to 9·3 in 1946,[3] that infant deaths due to syphilis decreased from 69 to 25 per 100,000 in the same time, and that in the eight years 1937–44 patients admitted to mental asylums because of syphilis fell from 7·1 to 5·8 per 100,000. Largely, no doubt, because of the war, the number

1. Report of the Ministry of Health for the Year ended March 31, 1946.
2. Freeble, C. R. jun., Robinson, A. *J. vener. Dis. Inform.* 1948, 29 307.
3. Heller, J. R. jun. *Ibid*, 1947, 28, 245.

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of new cases of syphilis placed under treatment substantially increased, but it is argued that many of these are accounted for by more efficient case-finding. The numbers of congenital syphilitics (stage unspecified) fell from 17,592 to 12,284 between 1941 and 1947.[4]

Not only by instruction of the public but also by instruction of the profession, a good deal more could be done in this country. Now that they have become the preserve of specialists, venereal diseases are too seldom mentioned in our medical meetings and have receded too far into the background of most doctors' minds. In another respect also we might do well to follow the American example—namely, in doing more to encourage venereological investigation. The fact that, in the past, venereal diseases have been mainly the concern of the local authorities has led to their comparative neglect at the principal places of medical research. The regional boards, in taking over the responsibility, have a great opportunity to promote inquiry as well as good treatment.

Annotations

EXAMINATION OF SPUTUM FOR MALIGNANT CELLS

THE search for malignant cells in the sputum is essentially a personal technique depending on the experience and judgment of the pathologist. It cannot be mass-produced and there is no sharply defined acid-fast colour reaction which will enable the examination to be entrusted to a junior technician. The pathologist himself must accept full responsibility for a report which may ultimately lead to the removal of a lung. A well-known chest surgeon once handed round to his class a pathological report and asked what was the most important item in it. After rejecting various proffered answers he replied, "the signature of the pathologist." There are pathologists who still take the safe line that malignant disease of the lung cannot be diagnosed under any circumstances by cytological examination of the sputum, but accumulated experience since the publication of Dudgeon and Wrigley's original paper has gone far to modify this pessimistic view. Lately Bergmann and others [5 6] have summarised a good deal of evidence which shows that cytological examination of the sputum for malignant cells will yield a positive diagnosis in a considerable proportion of cases (up to 72% in known positive cases), especially in apical lung carcinoma where the tumour may be beyond the reach of the endoscopist for bronchial biopsy.

There are two main types of sputum from which successful results can be obtained—the one containing small portions of malignant tissue and plaques of cells which retain some of the morphological appearances of the growth from which they have been detached; the other having only isolated malignant cells. Obviously the latter are much more difficult to interpret; indeed so difficult are they that a pathologist may often hesitate to commit himself even to a diagnosis of probability. But the contribution which he can make to the early recognition of malignant disease is so important that the acquisition of the necessary laboratory technique and experience is abundantly worth while. A routine cytological examination of all types of sputum forms a valuable training ground on which to base this experience. Bergmann and his co-workers indeed believe that all cells in sputum can be identified, and that neoplastic cells can with care be classified into their main varieties (squamous, adenocarcinoma, and small-cell carcinoma). Furthermore, examination of control films from operation material and bronchial biopsies will enable the pathologist to build up a personal technique which will stand him in good stead in many a difficult case.

The pathologist is now at a critical cross-road. Much of his work is being standardised so that relatively inexperienced laboratory staff can report with a plain "yes" or "no." The examination of sputum—and other secretions—for malignant cells is one of those tests in which painfully acquired experience alone counts. Unequivocal answers may be discouragingly infrequent, but any help which the pathologist can give in the diagnosis of an early, and probably operable, case of primary carcinoma of the lung will be welcome to his clinical and radiological colleagues.

THE RESEARCH-WORKER'S SALARY

THOSE engaging in full-time medical research are well aware that they could earn more in routine laboratory work or in clinical specialist practice. In a memorandum [1] published this week the Association of Scientific Workers observes that with the implementation of the Spens report on specialists' pay the research-worker's disadvantage will be accentuated. The association believes that without prompt action workers will drift into routine duties and that the flow of recruits will dwindle. (The report does not dwell on the position of doctors employed in the non-clinical departments of universities; their case, it says, has been fully explored at a conference of non-clinical professors.) Since the war, it says, the Medical Research Council and other bodies promoting full-time research have had difficulty in attracting young men and women; and there has even been internal competition for recruits between the full-time research laboratories of the M.R.C. and the Public Health Laboratory Service—an organisation directed by the M.R.C. whose workers perform both routine and research duties. Discrepancy between remuneration in these two divisions is already evident; and the Treasury is likely to agree that the staff of the Public Health Laboratory Service shall rank as specialists. "It is as unreal as it is unjust to rate separately the highly specialised medical 'back-room' experts and the 'front-line' specialists." The association does not seek to belittle the research-worker's advantages. "Thus the M.R.C. are in many ways model employers. They have succeeded in avoiding the dangers of bureaucracy; they have fostered a camaraderie among their staff; irritating administrative pin-pricks are conspicuously few; and the staff enjoy a high degree of independence." Research is a vocation, and economics are of secondary importance to the people engaged in it; "but the exigencies of present-day cost of living, the difficulty of bringing up a family, and the general wear and tear of post-war life, cannot fail to colour the undoubted intellectual attractions of a research career," particularly for those who like the idea of research but have not yet sampled it. "Further, except for the brilliant or fortunate few, a research worker encounters many bad patches—financial worries are hardly conducive to perseverance under these circumstances."

What is the remedy? In the association's view, each research-worker in a large group should be graded according to age, standing, and degree of scientific or administrative responsibility; this grading should correspond both in range and rate of ascent with the grading in respect of specialists' regular salaries in the National Health Service; and the equivalent N.H.S. salary should be

4. *Ibid*, p. 263.
5. Bergmann, M., Shatz, B. A., Flance, I. J. *J. Amer. med. Ass.* 1948, **138**, 798.
6. Shatz, B. A., Bergmann, M., Gray, S. H. *J. Lab. clin. Med.* 1948, **33**, 1588.

1. The Salaries, Status, and Recruitment of Full-time Medical Research Workers in Great Britain: a memorandum prepared by the Medical Sciences Committee of the Association of Scientific Workers. Obtainable from the general secretary of the association, 15, Half Moon Street, London, W.1.

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paid—less, say, 10% since the research-worker is spared the hurly-burly of the specialist's life. For senior workers there should be a chance of additional income on the lines of the distinction awards to specialists. Those with science qualifications who engage in full-time medical research should be paid on the same basis as those with medical qualifications; this principle is already pursued by the M.R.C., which, in further fulfilling it, may find itself in difficulty vis-à-vis the scientific civil service. "Nevertheless, we urge that only by increases which follow to a reasonable extent the upward trends in other specialist branches of the country's medical system, will all medical research workers be rewarded in a fair manner, and will an adequate supply of man-power be ensured for this essential service."

MOTH DERMATITIS

EVERY countrydweller knows that "woolly bear" caterpillars may cause dermatitis when handled, and in France the names "mal des bassines" and "mal des vers" have been given to dermatitis affecting girls employed in winding silkworm cocoons [1]; but it is not so well known that the hairs of some full-grown moths will also cause dermatitis. For instance, dermatitis due to contact with the hairs of the larva, cocoon, and imago of the brown-tail moth (*Euproctis chrysorrhœa*) has been reported in the U.S.A. several times, and to those of the cocoon of the same moth in England in 1884.[2] Strangely enough there seem to be no records of such dermatitis associated with the great plague of brown-tail moths in England in 1782. Both the brown-tail and the gold-tail (*E. similis*) moths have anal tufts of hair, and the females of both species shed theirs; as a kind of protective thatch, on their newly deposited ova. These hairs, freely handled by entomologists, have seldom been incriminated, but cases have been reported of dermatitis from the hairs of the gold-tail moth [3] and of its congener *E. flava*.[4] Dermatitis due to moths of the genus Hylesia, in South America, was first reported in 1918, and a spectacular outbreak [5] involving 31 of the crew of 45 on board the oil tanker *Wolfcreek*, was caused by a migrating swarm of female *Hylesia* (?) *tapabex* (the moths were badly crushed and their species therefore not exactly identifiable) off the coast of Venezuela on Feb. 16, 1947. The skin lesions appeared a few minutes to several hours after contact and were of two kinds: in the first there were groups of erythematous papules and papulovesicles on the arms, legs, and back, whereas the second was a more generalised urticaria chiefly affecting the flexor surface of the forearms and the front of the chest, abdomen, and thighs. The face, palms, soles, and mucous membranes were clear. The cause of the epidemic was not at first recognised; so the ship was placed in quarantine on its arrival at Boston. Those who had swatted the moths with their hands had also tried to kill them by exploding D.D.T. bombs, and at least one of these men had previously had a skin eruption after handling D.D.T. A fresh crop of cases on the ship's arrival at Boston on Feb. 22 followed an issue of fresh bed-linen. It was then discovered that moths had taken refuge in the linen cupboard and had stained the linen and shed hairs on it. Patch tests with stained linen and with hairs clinched the diagnosis. Removal of the patient from the source of contact, a soap and water bath, a change of clothing, and the application of an alkaline wash relieved the symptoms in 24 hours, and the lesions disappeared in 4–7 days. Adrenaline and anti-histamine drugs were tried but apparently had no effect.

1. See *Lancet*, 1900, ii, 1242.
2. Thresh, J. C. *Lancet*, 1906, ii, 291.
3. *Lancet*, 1908, ii, 1466.
4. Mills, R. G. *Chin. med. J.* 1923, **37**, 351.
5. Hill, W. R., Rubenstein, A. D., Kovacs, J. jun. *J. Amer. med. Ass.* 1948, **138**, 737.

A LESS TOXIC STREPTOMYCIN

Two of the drawbacks to streptomycin are toxicity and resistance. At first it was thought that impurities might be responsible for most of the toxic effects, but even when the pure substance was obtainable they were still observed both clinically and in animal experiments. It was hoped that, by slightly modifying the molecule, toxicity and resistance might be altered without interfering appreciably with antibiotic activity. In 1946 the catalytic hydrogenation of streptomycin to dihydrostreptomycin was described by Peck and his co-workers,[1] and during the last year extensive laboratory and clinical studies on this substance have been made in various centres in America. Rake and his colleagues [2] at the Squibb Institute for Medical Research, New Jersey, have shown that for most strains of *Myco. tuberculosis* there is little in-vitro difference between the activities of streptomycin and of dihydrostreptomycin, though the latter is somewhat less active against *Salmonella schottmülleri* and *S. typhosa*. Edison and her co-workers [3] at the Merck Institute for Therapeutic Research, New Jersey, have confirmed the observations on *M. tuberculosis* and found no substantial difference in the antibacterial activity of the two drugs when tested against a variety of other pathogenic organisms.

Unfortunately, hydrogenation has no effect on drug resistance; organisms resistant to streptomycin are also resistant to dihydrostreptomycin. But the Merck workers did find that the chronic neurotoxicity of streptomycin, which is a serious obstacle to its clinical use, is greater than that of dihydrostreptomycin. When the two drugs were given to cats in equiactive doses, ataxia and other vestibular disturbances were delayed and were less severe in the dihydrostreptomycin group: these animals also lost much less weight and showed fewer signs of toxicity than those receiving streptomycin. Similar observations were made by Hobson et al. [4] at Cornell University. Biochemical, haematological, and pathological studies showed little difference between groups of dogs and monkeys treated with streptomycin and with dihydrostreptomycin. It is generally recognised that slight changes in chemical composition may alter the capacity of a drug for producing sensitisation. Dihydrostreptomycin, with a greatly altered polar group, might be expected to differ significantly from streptomycin in this respect. Hobson and colleagues found that dihydrostreptomycin is well tolerated by patients who are hypersensitive to streptomycin. They also showed that it is less neurotoxic in man than the parent substance. Vestibular damage appeared later in patients given 5 g. of dihydrostreptomycin daily than in those receiving 3 g. of streptomycin. Disability resulting from vestibular dysfunction was also less in the dihydrostreptomycin patients. Renal damage, which has been observed in patients receiving streptomycin, has also occurred in those given dihydrostreptomycin. To determine whether the diminished toxicity of dihydrostreptomycin was due to lower concentration in the blood and other body fluids, Levin and others [5] at the Mayo Clinic compared the absorption, excretion, and distribution of dihydrostreptomycin and of streptomycin in various body fluids. Data obtained were very similar for the two drugs. Dihydrostreptomycin can be found in significant quantities in the pleural fluid and the cerebrospinal fluid after intramuscular injection.

1. Peck, R. L., Hoffhine, C. E. jun., Folkers, K. *J. Amer. chem. Soc.* 1946, **68**, 1390.
2. Rake, G., Pansy, F. E., Jambor, W. P., Donovick, R. *Amer. Rev. Tuberc.*, 1948, **58**, 479.
3. Edison, A. O., Frost, B. M., Graessle, O. E., Hawkins, J. E. jun., Kuna, S., Mushett, C. W., Silver, R. H., Solotorovsky, M. *Ibid*, p. 487.
4. Hobson, L. B., Tompsett, R., Muschenheim, C., McDermott, W. *Ibid*, p. 501.
5. Levin, L., Carr, D. T., Heilman, F. R. *Ibid*, p. 531.

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A clinical investigation of dihydrostreptomycin in tuberculosis was undertaken by Feldman, Hinshaw, and their group at the Mayo Clinic [6] during 1948. They had previously shown that in experimental tuberculosis in guineapigs, due to a human strain (H 37 Rv), dihydrostreptomycin is as effective as the parent substance in prolonging the survival-rate of the infected animals and in limiting the spread of the infection.[7] Their clinical material was limited to only 14 cases, but they were convinced that the activity of the dihydro compound was similar to that of streptomycin. They were also impressed with the diminished toxicity of dihydrostreptomycin. Thus they could administer it to patients in doses of 2–3 g. daily for sixty days or longer with little danger of producing vestibular dysfunction. They also observed that the drug is tolerated by some patients who are highly sensitive to streptomycin. The Mayo Clinic workers did, however, note that in cases of tuberculous meningitis intrathecal therapy produced irritation of the cord and a block in the cerebrospinal fluid. Some irritation at the site of intramuscular injection was observed in some patients, but was no worse than that after the injection of streptomycin. Another 12 cases of pulmonary tuberculosis treated with dihydrostreptomycin are reported by Hobson and colleagues.[4] They also confirm the diminished neurotoxicity of the drug in man and consider that the therapeutic results are as good as those obtained with streptomycin.

These preliminary clinical reports are encouraging, though they need to be confirmed on a larger series of cases. There seems to be no doubt about the diminished neurotoxicity of dihydrostreptomycin and its ability to replace streptomycin in hypersensitive patients. It might therefore be preferable to streptomycin for patients who require large doses or long courses. We still know little about the therapeutic effectiveness of streptomycin in small doses—the precise ratio of the toxic dose to the optimal therapeutic dose has not yet been established. It is thus important that experience should be gained on the effectiveness of dihydrostreptomycin in dosages that are well tolerated for long periods.

ADRENALINE AND ITS NEAR RELATIONS

IT has long been known that adrenaline is the active substance obtained from extracts of the suprarenal medulla. The *lævo*-isomer is the one found in the gland and this has much greater pharmacological activity than the *dextro* compound. Commercial *l*-adrenaline is now usually prepared synthetically, and to maintain stability it is essential to have it in acid solution and advantageous to include a stabiliser such as sodium or potassium metabisulphite.

The chemical mediator (or mediators) liberated by adrenergic nerves has not yet been identified with certainty. The evidence of experiments with isolated frogs' hearts and perfused rabbits' ears has supported the view that this substance is adrenaline. But the findings with other mammalian tissues suggest that adrenaline is not the only substance liberated. It is not yet known how adrenaline is formed in the body but information is accumulating. A second phenolic hydroxyl group may be introduced into the tyrosine molecule, thus forming dihydroxyphenylalanine; decarboxylation then occurs yielding hydroxytyramine, and the introduction of the OH group into the side-chain follows to form the primary sympathomimetic amine, noradrenaline. The last stage of adrenaline formation is the N-methylation of noradrenaline. Since adrenaline occurs as the *lævo*-isomer in the adrenal medulla, one might expect that if there were other similar natural compounds they would also occur as the *l*-isomers. The production of *l*-noradrenaline last year has made it possible to compare this substance with sympathin liberated by, or contained in, adrenergic nerves. In an adrenal tumour about ten times as much *l*-noradrenaline as *l*-adrenaline has been detected, and it may be that noradrenaline as well as adrenaline is present in the normal adrenal medulla.

So far as we know, adrenaline (which may also be called methyl-noradrenaline) and noradrenaline are only absorbed adequately when given by injection, and even then absorption is slow. The instability of these substances is said to be due to the presence of the three-OH groups. The molecule of ephedrine differs from that of adrenaline in the absence of two hydroxyl groups and the presence of an extra methyl group in the side-chain, both of which differences tend to make ephedrine stable. Hence ephedrine is effective when given by mouth and its action lasts longer than that of adrenaline. A stage further in stability is reached when the three-OH groups of the adrenaline molecule are omitted, the N-methyl group is lost (as in noradrenaline) and the extra methyl group is added (as in ephedrine). The resulting compound—amphetamine or 'Benzedrine'—is volatile and may be inhaled to produce vasoconstriction in the nose. Both amphetamine and ephedrine are derivatives of isopropylamine, and are not inactivated by tissue amine oxidase.

Returning again to the adrenaline molecule, noradrenaline results if the N-methyl group is lost. But if the N-methyl group is replaced by a N-isopropyl group, 'Aleudrine' or isopropylnoradrenaline is produced. This compound, when tested on animals, is vasodepressor in all doses but produces the typical tachycardia. Its therapeutic importance lies in the fact that it is many times stronger than adrenaline as a bronchodilator and can be administered by mouth.

6. Feldman, W. H., Karlson, A. G., Hinshaw, H. C. *Ibid*, p. 494.
7. Hinshaw, H. C., Feldman, W. H., Carr, D. T., Brown, H. A. *Ibid*, p. 525.

FEWER N.H.S. PRESCRIPTIONS?

IN Middlesex the number of National Health Service prescriptions grew steadily, at the rate of about 100,000 a month, from 511,031 in July to 915,931 in November. Then last month the total receded by nearly 42,000 to 874,077. Some may attribute the decline to the season. Or it may be that doctors are now giving fewer and larger prescriptions, or that patients, weary of waiting in surgeries, are sometimes buying medicines themselves or going without. But it is possible that initial curiosity and desire to test the new service is becoming exhausted. The experience of one county in one month is not proof that demand has reached or passed its peak; but it may be a hint.

BETTERMENT

IT will be remembered that the Spens Committees made their recommendations in terms of the 1939 value of money. "We leave to others," they said, "the problem of the necessary adjustment to present conditions, but we would observe in this connexion that such adjustment should have direct regard not only to estimates of the change in the value of money but to increases which have in fact taken place since 1939 in incomes in other professions." The British Medical Association has now received a report from an expert who argues that if the professional classes' cost-of-living figure in 1938 is taken as 100, the appropriate figure for today is 185. He points out that it has risen by 35 points since 1946 when the Ministry of Health decided that 20% should be added for betterment. Reasons for an increase will be put forward by a deputation from the Joint Committee of Consultants and Specialists and the General Medical Services Committee.

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Special Articles

PREVALENCE OF TUBERCULOSIS IN WESTERN GERMANY

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IN September, 1947, we visited the British Zone of Germany and Berlin at the request of the Foreign Office to investigate the prevalence of tuberculosis. In our report [1] we concluded that the situation in the British Zone (excluding Berlin) was not alarming; that the war-time rise in tuberculosis mortality had been checked; and that the levels of tuberculosis mortality in the individual Lands of the Zone compared favourably with those in parts of Great Britain and other European countries. We concluded also that the much advertised increase in morbidity, based on notifications, was largely a paper increase. We considered the position in Berlin, on the other hand, to constitute a grave problem, with a high level of tuberculosis mortality, which, however, showed evidence of a commencing decline.

Some recent publications support these findings. The most important is the report of a mission directed by the secretary of the United States Army "to investigate the incidence of, and recommend control measures for tuberculosis among the German civilian population." Reports to the Department of the U.S. Army from German sources had suggested that a significant rise in the prevalence of tuberculosis had taken place in the Western Zones of Germany; and information was wanted on the nature and extent of this rise. The mission, headed by Dr. Esmond R. Long, visited Berlin and the U.S. Zone of Germany in February of this year, and their findings have been published.[2]

The conclusions of the Americans regarding tuberculosis trends in the U.S. Zone (excluding Berlin) are similar to our own for the British Zone. They found that the tuberculosis death-rate, after a war-time rise, was again declining, and in most parts of the Zone was approaching the pre-war level. The mission agreed that death-rates are the most sensitive and valid index of tuberculosis trends, and expressed disagreement with, and surprise at, the emphasis laid by German specialists on the reported case-rates of tuberculosis as an index to the extent and trend of the disease.

An unsigned article by a German doctor [3] supports these conclusions and deplores the issue of alarmist reports based on unreliable morbidity statistics. He concludes: "Conditions are bad enough; there is no need for exaggeration, which in the long run harms instead of helping us."

However, a report by Dr. Ickert,[4] a German physician, returns to the previous conception, which attached great importance to morbidity statistics. This report is sponsored by the German central committee for tuberculosis control in the British Zone, and for that reason alone merits serious analysis. Unfortunately the book is so full of errors as to make bewildering reading. Thus, in support of the argument that tuberculosis prevalence is increasing, the totals of sputum-positive cases on the dispensary registers in successive post-war years are compared, and Ickert contrasts a figure of 11,484 open cases in 1945 with 42,126 in 1947. The 1947 figure, however, is for the whole British Zone, whereas the 1945 total excludes North Rhine-Westphalia, for which Land no 1945 figures were available, but which contains half the population of the Zone. He compares in a similar way figures for cases of all types on the registers for these years. Apart from the major error just indicated, the validity of the comparison is seriously affected by the increase in dispensary activities, including case-finding, from the chaotic final war year through succeeding years. Turning to the mortality data, in his presentation of tuberculosis death-rates for the whole British Zone, Ickert gives figures of 70, 89, and 77 deaths per 100,000 for 1945, 1946, and 1947 respectively—showing, therefore, higher rates in 1946 and 1947 than in 1945. But here again 1945 figures for North Rhine-Westphalia are not available, and it is impossible to see how he has reached the total figure of 70 for 1945. Actually, in two of the three Lands other than North Rhine-Westphalia, the rate fell between 1945 and 1946. Finally, it is stated in the conclusions that the tuberculosis mortality in males is still increasing; but, though full statistical tables are given at the end of the report, we can find no figures to justify this statement.

In other respects Ickert's book performs a useful service. Some of the statistics given in the tables differ from the provisional ones given to us a year ago from German sources, and one can assume that these are now the definitive statistics; furthermore, figures for the whole of 1947 are now given. The tabulations of tuberculosis mortality in the British Zone show a more definite fall between 1946 and 1947 than we could demonstrate; this fall took place in each of the four Lands. The rate of 77 deaths per 100,000 population for the whole British Zone in 1947 may be compared with that of 54 (provisional figure) for England and Wales excluding London (1947), of 80 for Scotland (1947), of 124 for Eire (1947), and of 81 for France (1946). The rate of 80 for Hamburg in 1947 compares with that of 69 for London (1947), 129 for Glasgow (1947), and 163 for Dublin (1947); it compares with 72 for Paris (1947), 71 for Brussels (1947), and 159 for Rome (1946).[5] Ickert's figures also show a consistent decline in tuberculosis mortality in the Lands of the U.S. Zone between 1946 and 1947.

The tuberculosis mortality figures for the first half of 1948 in the British Zone, reported from the German Statistical Office, have just been made available to us through the courtesy of Brigadier Strelley Martin, public-health adviser to the British Military Governor, Germany. By comparison with previous corresponding half-years, they show a continuation of the post-war fall in the tuberculosis death-rate in the British Zone, though at a reduced rate of decline:

Form of Tuberculosis		*Annual death-rates per 100,000* 1946*	1947	1948
January–June	Pulmonary ..	85	68	65
	Other	19	17	13
	All	104	85	78
July–December	Pulmonary ..	58	54	..
	Other	15	15	..
	All	73	69	..

* Comparable figures for the half-years of 1945 are not available for all Lands, and those available are not completely reliable owing to the conditions then prevailing.

The falling rate from 1946 to mid-1948 is evident in each Land of the British Zone, as shown in the accompanying figure.

These statistics give no support to the sensational statements that were being made in 1947 on the basis of exaggerated estimates of the prevalence of tuberculosis.[6] Nor do the fears expressed by some, that the apparent rise in morbidity at that time heralded a further calamitous rise in mortality in the near future, seem to have been well founded. None of the arguments and the

1. Daniels, M., Hart, P. D'A. Tuberculosis in the British Zone of Germany. London: H.M. Stationery Office. 1948.
2. Tuberculosis, U.S. Zone Germany, Special Report of the Military Governor, Germany (U.S.), May, 1948; and *Bull. U.S. Army med. Dept*, 1948, 8, 564.
3. *Tuberk Arzt*. 1948, 6, 486.
4. Ickert, F. Die Tuberkulose in der Britischen Zone. Hanover, 1948.
5. *W.H.O. epidem. vital Stat. Rep.* March, 1948.
6. *Manchester Guardian*, Berlin Correspondent. June 4, 1947.

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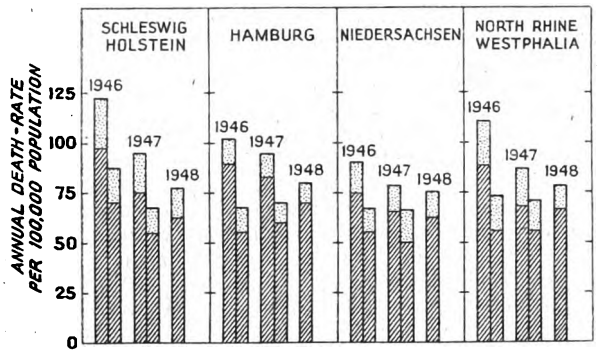
detailed morbidity figures presented by the German doctors to support this forecast is any more valid now than it was a year ago. War-time and post-war statistics from France and Belgium, for instance, show steadily increasing dispensary case-totals concurrently with a falling tuberculosis mortality. Thus, in Belgium the number of cases on tuberculosis registers increased from 43,900 in 1940 to 131,380 in 1943, but tuberculosis mortality reached a peak of 130 in 1941, since when it



Half-yearly mortality from tuberculosis in 1946-48 in Lands of the British Zone, Germany; left-hand columns of 1946-47, January–June; right-hand columns of 1946-47, July–December; 1948 columns, January–June. Hatched portions, pulmonary tuberculosis; stippled portions, other forms of tuberculosis.

has steadily fallen, reaching a rate of 70 in 1947. The death-rates remain the most accurate index of tuberculosis trends.

These comments are not intended to detract from sympathy for the German people. Although tuberculosis is not so prevalent as has been claimed by some, and is not so high as in many other countries, the position is serious enough to give no grounds for complacency. A declining mortality at the present time offers no sure guarantee that this will continue. Moreover, we realise that the Germans are living in conditions which would be expected to favour the spread of tuberculosis; improvement of housing and of the food situation should have a beneficial effect on the tuberculosis-rates, as it would in other countries. However, it must be evident that faulty statistical analyses cannot assist the Germans in assessing the true position. Before 1933 they had a high reputation in statistical records and analysis; it may be hoped that gradually they will make good the deterioration of the Hitler years.

SUMMARY

Judged by death-rates, the tuberculosis situation in the British Zone (excluding Berlin) improved from 1946 up to mid-1948.

"... One word about pillows. Every weak patient, be his illness what it may, suffers more or less from difficulty in breathing. To take the weight of the body off the poor chest, which is hardly up to its work as it is, ought therefore to be the object of the nurse in arranging his pillows. Now what does she do and what are the consequences? She piles the pillows one a-top of the other like a wall of bricks. The head is thrown upon the chest. And the shoulders are pushed forward, so as not to allow the lungs room to expand. The pillows, in fact, lean upon the patient, not the patient upon the pillows. It is impossible to give a rule for this, because it must vary with the figure of the patient. But the object is to support, with the pillows, the back *below* the breathing apparatus, to allow the shoulders room to fall back, and to support the head, without throwing it forward. The suffering of dying patients is immensely increased by neglect of these points. And many an invalid, too weak to drag about his pillows himself, slips his book or anything at hand behind the lower part of his back to support it."—FLORENCE NIGHTINGALE, *The Art of Nursing*. Revised edition. London, 1946.

The Act in Action

5. HOSPITAL OUTPATIENTS AND ADMISSIONS

THE hospitals are now dealing with many patients—particularly women and children—who are in need of expert advice and even admission but would not have attended if there had been no National Health Service. Since July 5 a heavier burden has been borne by the consultative services. General practitioners without the time—and possibly the wish—to undertake detailed examinations or time-consuming treatments are sending more people to outpatient departments; and the Act makes these departments mainly responsible for issuing appliances.

OUTPATIENTS

Even before the start of the service, outpatient attendances had been rising towards the pre-war total.[1] In London since July 5 this total has been rapidly reached and surpassed. In 1947 the London Hospital had 84,928 new outpatients with 475,240 attendances: last year the figures rose to 95,963 and 519,901. At King's College Hospital attendances in November, 1947, numbered 26,000; last November they totalled 35,000. At Edgware General (then Redhill County) Hospital, in the December quarter, 1947, there were 11,026 new cases and 42,088 attendances; last year the comparable figures were 12,689 and 50,432. The actual increase may be somewhat greater than these figures suggest; some hospitals used to keep on as outpatients people who were not strictly in need of hospital treatment but who could not afford the fees of a general practitioner or the cost of medicines; this work is now ended.

In response to the new demand, clinics have been duplicated and in some cases triplicated. A number of hospitals already have an appointments system; the virtues of such a system have been heavily underlined since July 5, and the Minister of Health has just recommended its general introduction "as a matter of urgency." He also urges that clinics should be held at times meeting local convenience, that where necessary departments should be redecorated and equipped with comfortable chairs, and that if possible a canteen should be provided. For the hospital, appointments assure that the department—which is often too small—does not become overcrowded; the patient and his notes can be made to reach the consultant at the right time; and there is a steady flow of patients to the ancillary departments.[2] For the consultant such a system has the merit of enabling him, first to judge how long he will be detained, and secondly to group patients with particular disorders, for teaching or other purposes. To the patient it means that the risk of having to hang about is minimised; at King's College Hospital the average waiting period has fallen from $1^1/_2$ hours to half an hour.

Appointments have their drawbacks. Often the interval between fixing the appointment and seeing the patient is a week or less; but sometimes it is a month or more, and during this interval the patient's condition may become urgent. That patients occasionally prefer to be seen without this delay, though at the cost of immediate inconvenience, is indicated in cities where some hospitals are operating the system and others are not. To the latter comes a steady trickle of patients who would have attended a hospital in the first group but for the waiting period. Moreover, the whole system of appointments is thrown out of gear if the consultant is unable to attend or even if he is late. Time may be

1. King Edward's Hospital Fund for London: Statistical Summary of the Income, Expenditure, Work, and Costs of 159 Hospitals for 1947. See *Lancet*, 1948, ii, 834.
2. King Edward's Hospital Fund for London: Some Observations on Hospital Admissions and Records. London, 1948.

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wasted, too, if a patient does not arrive at the appointed time; and at King's College Hospital patients due to attend those special clinics where each consultation takes over half an hour are asked to confirm on the previous day that they will attend. However, its users in general welcome the practice.

The cost in labour and money is not negligible. At King's College Hospital, in a department dealing with 45,000 inquiries and 30,000 appointments a month, 9 clerks are employed (including 4 typists, of whom 2 are part-time); of these, 6 were taken on to deal with appointments. In addition, 8 clinical receptionists are engaged, their main duties being to get the patient and his notes to the doctor, and to conduct the patient from one department to another.

Some consultants, impressed by the triviality of many of the cases now referred for their opinion, reason that this pressure should be eased by the appointment of more registrars and clinical assistants. In a few areas administrators believe that, now that the hospitals are unified, overlap between the clinics at nearby hospitals should be ended; and in the more compact areas thought is being given to the establishment of a single consultative centre at the hospital most conveniently situated for patients and possessing the best ancillary services.

ADMISSIONS

Some measure of the unsatisfied demand for places in hospital is given by the experience of the Emergency Bed Service in the last six months.[3] At the beginning of December applications were about three times as numerous as in 1947, and were still increasing. The difficulty, in the experience of the E.B.S., is greatest with cases which are, or might become, chronic; but it has also proved hard to gain admission for other groups, notably babies. On another page a correspondent complains of the offhand way in which applications for admission are sometimes dealt with; and, mindful that this criticism has often been justified, some hospitals are setting up admission offices to deal more swiftly—and politely—with patients and their family doctors.

Hospitals are increasingly alive, in the changed circumstances, to the necessity for knowing exactly how many are awaiting admission. Waiting-lists, the significance of which varies from one hospital to another, do not always fluctuate with the demand on beds. At the London Hospital the length of the list has not changed greatly since the appointed day, whereas at King's College Hospital it grew from 2700 at July 5 to 3927 at Dec. 1. The longest lists now are commonly for admission to the following departments: ear, nose, and throat (particularly children for tonsillectomy); gynæcological; orthopædic; and general surgical (patients whose names are down for operation on varicose veins may have to wait 4 or more years).

Unless the hospital takes the trouble to keep in touch with patients, the number actually waiting to come in will be less than the list indicates. In the time between his name being placed on the list and his being sent for, the patient may leave the district or be treated elsewhere; he may die, or he may recover. If unaware of this, hospitals sending for patients at the last minute find that beds are being wasted. At some centres letters now go out from time to time to make sure that admission is still required; and this token of being at least remembered usually heartens the recipient. At other places the patient is told a week or so in advance the date on which a bed is being reserved for him, and this gives him time to confirm that he will be coming and to make personal arrangements. At some hospitals—Edgware is one—specialists find it possible to inform outpatients at their first attendance when they will be admitted, even if the date is six or eight months ahead. At this hospital children referred for tonsillectomy are not seen as outpatients until about a week before a bed can be found for them; this makes it as certain as possible that when admitted the child will really need operation and will be fit for it.

If general hospitals dealt only with patients from the waiting-list no bed need be empty at night. But, as they have to take an unpredictable number of emergencies, some beds are inevitably unoccupied; and usually a bed occupancy of 85% has been about the average. Some general hospitals, however, are now averaging 90%; and one large teaching hospital in London (which has a ratio of nurses to patients far below 1 : 1) has achieved and sustained an average of 97%. This has demanded considerable effort and good will, since patients may be admitted at night to beds, not in the appropriate wards, but where they can be found; and the following morning these patients have to be sorted out. At this centre it is believed that 10% vacancy is probably the optimum.

At the London Hospital the unsatisfactory midnight return of bed-state has been superseded by a board giving minute-to-minute information on beds occupied and vacant; and at King's College Hospital a similar board is to give the name of each inpatient.

Can better use be made of beds by closer integration of hospitals? It has been suggested that beds could be more fully used by free interchangeability of patients between hospitals in an area. First steps have already been taken in this direction; in the Bromley area a resident obstetrical officer has been appointed for duty in all the hospitals under the management committee. The drawback to interchangeability is that a patient seen as an outpatient by one consultant might be admitted to the ward of another in a different hospital; and to this both specialists might very reasonably object. To overcome this a senior staff common to all the hospitals of the area could be appointed; but this would reduce the choice of consultants—a choice which to practitioners and others seems desirable.

Perhaps a more promising approach could be made by trying to get "the right patient in the right bed." Consultants visiting some outlying hospitals have been impressed by the wastage of nursing skill in the admission and retention of patients in hospitals where their condition cannot be properly investigated or treated. The converse does not necessarily hold: there is a case for retaining in beds associated with the principal centres some chronic sick not in need of special investigation or treatment, both for the instruction of students and nurses and because of the difficulty of staffing hospitals which deal exclusively with non-acute conditions.

What of the beds standing empty through lack of staff? It has been too readily assumed that these beds are closed because too few recruits to nursing are coming forward. Yet last September 121,000 nurses and midwives, trained or in training, were employed full-time in the hospitals of England and Wales, compared with 115,500 in June, 1947, and 118,000 last June. The number employed part-time rose by 9000 in the fifteen months from June, 1947, and by 2000 between last June and September. Part of this increment has, however, been used to introduce, where possible, a 96-hour fortnight—which may be expected to stimulate further recruitment.

In more than one area the main trouble is that no further resident nurses can be taken on until: (1) proper accommodation has been found for those already employed; and (2) new accommodation has been bought or built for further numbers. Thus in an area with 400 of its 1600 beds unstaffed candidates are actually being turned away because no living accommodation can be found for them.

Management committees often feel that they are poorly armed for the struggle to obtain this additional accommodation and thus to bring more beds into

3. Peers, R. E. *Lancet*, 1948, ii, 1026.

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operation. Prefabricated buildings can be set up only where a site is free; and in bidding for existing buildings regional boards can normally offer only the amount named by the district valuer—an amount which is almost always below the selling-price. Compulsory purchase is a long process, and the power is exercised only exceptionally; while section 2 of the Acquisition of Land (Authorisation Procedure) Act, 1946, which confer temporary powers for speedy acquisition of land in urgent cases, is not applicable here.

Mr. R. C. Millward, secretary of the Bromley group, points out that shortage of nurses is acutest in hospitals which can offer no training; the first need is to bring these into training schemes, which can be done by grouping hospitals; and the allocation of beds to the different departments may in some districts be greatly influenced by the requirements of the General Nursing Council.

THE FUTURE

It will be many years before hospitals can meet all demands. Meanwhile the guiding principle must be to send no-one to the outpatient department who can be treated satisfactorily outside hospital, to admit no-one who can be investigated and treated as an outpatient, and to retain no-one who is fit for discharge or convalescence. The most prominent trend in recent months has been towards making the outpatient department the gathering-point of all the more complex cases seen in general practice. If this trend is to be arrested, the public will have to learn that specialist services should be used with discretion, and the practitioner will have to be given leisure and encouragement to retain responsibility. If the trend is to go unchecked, a two-tier system will have to be evolved in each outpatient department, clinical assistants or registrars examining the trivial cases, and consultants concentrating on the serious.

In the wards awareness of urgency is already evident in tentative moves towards establishing "hostels" where walking patients admitted for a few days' investigation could be housed without full ward service.[4] In some areas, too, medical officers of health have been drawn into the management of hospital affairs, which helps to ensure that the fullest possible use is made of the local health authority's resources. In particular this liaison makes sure that the chronic and elderly sick are discharged as soon as the authority can take charge.

4. See leading article, *Lancet*, 1947, ii, 726.

"... a sleight of hand artist can divert our attention from one move he makes by making at the same instant another move that is spectacular and preoccupying. 'Look at the dicky bird!' is in effect a blinding command. ... Science provides us with instruments of entrancing accuracy, with oil-immersion lenses and potentiometers and spectrographs and X-rays, all of which are superbly efficient for seeing parts of the total picture. But even these remarkable instruments do not excuse us from the task of looking at the whole picture or of deciding what part of the total picture is worth looking at. Quite to the contrary, they make it seductively easy to look at something merely because it can be seen. Now even if an instrument of precision will automatically register, measure, and record a singularly active and colorful dicky bird, we may be giving all our attention to what is no better than a dicky bird for all its beautiful verifiability. If I may offer a facetious suggestion—why not add one more word to our medical dictionaries—*ornithographs*, a collective term to describe all the pictures of the dicky birds that deflect our attention from what is important, by substituting mere precision for true comprehensiveness of observation? Wrapt attention to the part is the best guarantee that the whole will be ignored. Of course when the part explains the whole, attention to it is an elegant procedure, but when the part obscures the whole, preoccupation with the part exemplifies misleading exactitude, and science at its worst."—Dr. ALAN GREGG, in an address to the American College of Physicians, April 21, 1948.

In England Now

A Running Commentary by Peripatetic Correspondents

SOME students of the generation before mine used to tour the wards with a bottle of ink suspended from the lapel of the coat and with a quill pen in hand or behind the ear. We used fountain pens. The point I wish to make is that, throughout our clinical training, emphasis was laid on observing and writing things down. As a result I find that most of my hospital contemporaries work with pen and paper (or thin cardboard) always at hand. A G.P. always has to see to a large number of things small in themselves but important to patients and to the smooth running of practice. Am I wrong or do I detect a lamentable deterioration among my juniors and betters in this salutary habit? It is so easy to take that telephone call which interrupts a consultation, make a mental note that Mrs. Somebody wants a visit, and forget to put it down on the visiting-list; or to carry out that efficient antenatal examination, dismiss the patient, and find that you can't remember her name, address, or blood-pressure; or to do that tricky little minor operation which was such fun and so successful and make no clinical note about it. What a bore it is when some insurance company or Government department wants a report about the affair six months later and you can't remember dates or details. I submit that the case for writing things down, always a strong one, is under the N.H.S. Act absolutely unanswerable.

* * *

E.B.S.: A DIRGE OR THRENODY

Beds, we adjure ye!
Say the girls of Old Jewry.

Sorry, we have none,
Says Reception at London.

We're full up too,
Says the Royal Waterloo.

Not a space to be seen
In all Bethnal Green.

Harden your hearts,
Says the houseman at Barts.

Moaning and snarls
Are all from St. Charles.

Surely some hospital must have a bed?
Here comes a G.P. to chop off my head.
(Chop, chop, chop, chop, that one's dead!)

* * *

Candidates in the recent M.R.C.P. examination, expecting inquiries into abstruse biochemistry or the most recent advances in medicine, must have rubbed their eyes at the homeliness of the questions.—Discuss the differential diagnosis of a fainting attack in a young man. On what evidence would you decide that a child of 18 months was normal both mentally and physically? Describe the treatment of hiccough.—More appropriate, they might have thought, for the layman's smattering acquaintance with domestic medicine; and indeed, though the average layman would not have thought of progressive cerebral thrombo-angiitis obliterans, which was the first cause of fainting advanced by one candidate, and would not have known about hypersensitivity of the carotid sinus, he would probably have remembered the possibility of a tight collar in this connexion. But perhaps in these days of sartorial indifference tight collars are *vieux jeu*. One aspirant, before plunging *in medias res*, asked, "What is a 'young man' and what is a 'fainting attack'?"; an admirable opening, though unhappily he omitted to answer his own questions. Ultimately we were left with the conclusion that the modern young man, while fully up to date with all the results of contemporary pathology, also embodies the swoons and vapours of the early Victorian miss.

The normal child of 18 months? I now picture the dismay of fond and anxious parents confronted with the exacting demands of the experts. On the one hand, insistence on all the positive virtues to establish a perfection to which surely no normal child could ever attain: on the other hand, the necessity to exclude all the horrors culled from the depths of pædiatric morbidity.

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It was necessary to secure "a careful history" comprising at least three generations. "The child, on questioning (*sic*) may be found to have a hæmophiliac great uncle." Gargoylism, tuberose sclerosis, Tay-Sachs amaurosis, Laurence-Moon-Biedal syndrome, all of these must on no account be overlooked. An exhaustive clinical examination should include manipulation of the head for egg-shell crackling and "seeing if you can tie the child in a knot" to be sure there is no amyotonia. The claimant to normality must be subjected to every possible investigation, including, of course, a tuberculin test and a Wassermann reaction but also electrocardiography and encephalography. And a little psycho-analysis must not be forgotten.

The unfortunate sufferer from hiccough (no purist rebukingly corrected this to hiccup) must be prepared for bilateral phrenicectomy. Perhaps the scornful doctor was justified in presuming that all the homely remedies had already been tried in vain before his skill was requisitioned, since a somewhat condescending reference to these was followed by the grudging concession that sometimes this or that may prove successful. Am I right in supposing that the recommendation of a key put down the back is a confusion between hiccup (hiccough) and epistaxis? I think I realise what the candidate was aiming at in his advice to drink a glass of water backwards or upside down, though I sympathise with the bewilderment of a sufferer attempting to follow that instruction literally. Nobody mentioned forcible traction on the tongue. Does that method possess the imprimatur of Hippocrates? Even if it does, I hold no brief for it. Very early in my career I applied it in the case of a young female relative. I do not remember if it cured her hiccup (hiccough) but I remember other consequences which have restrained me from ever repeating the procedure.

* * *

As a Membership candidate of some years' sitting I deplore both the number and the quality of the influx into our regular quarterly meetings. As a *Why not chance it* boy I find the *I can get it* entry rather poor stuff. If this overcrowding goes on I can foresee the day when all G.P.'s will be failed fellow-travellers and will bore one another with tales of how they missed "Some aspects of the left adrenal" but rattled off on the "red marrow." Instead of attending to the simple needs of their patients they will be itching to diagnose by a glance and the sound of the traffic at Hyde Park Corner. But why should a chance-it G.P. worry?

* * *

CHAUCER: 1949 MODEL

A practisour there was with penne in fyste,
He had four thousand pacions on his lyste
And doctored them right spedely; to each
He gave two minutes, cutting short their speche,
Writing them scripte in Latin most impure.
He had a verray pretty signature
Which none coude rede, but noöne ever tryed.
He had a motor carre in which to ryde
And eke a bagge to hold his stock-in-trade
—Divers certificates of every shade—
These he dispensed with a lavish grace,
Writing the details in the appropriate place.
With these and him his pacions were content,
He had no neede for any instrument.
He took no trouble, but he gave none
So he stood high with high-ups everyone,
Small wonder all came floccynge to his door
He was a parfit general practisour.

* * *

If the intrinsic value of a doctor is to be measured by the number of those who feel the better for his ministrations, I wonder which of us could hold a candle to Tommy Handley, who doctored, among so many others, the doctors themselves? There are, I suppose, a benighted few to whom ITMA was not the most important event in the week, but many of us may well be wondering how we are to carry on without it. Meanwhile we must comfort ourselves with the certainty that Tommy is already setting the table in a roar with his sure, quick-fire comments in the place where all good jesters go.

Letters to the Editor

HOSPITAL MANNERS

SIR,—Having lately been an inpatient for five weeks in my own London teaching hospital (I am an ex-Service student) I can confirm that even in the best hospital there is still room for improvement in hospital manners. I have been disappointed to see no practical suggestions, apart from your admirable leading article of Nov. 13, emerging from the recent correspondence on this subject.

My opinion is that most faults in hospital manners are caused by ignorance of two kinds: firstly, the patient never knows enough about either the hospital or his own progress, and secondly, the "hospital" (i.e., its staff of all kinds) know too little about their patients' viewpoints. If this mutual ignorance is eliminated, other causes of complaint—whether because of unsuitable administration, equipment, or buildings—will also be far more easily revealed. I suggest the following measures:

1. It should hardly be necessary for all staff (doctors, nurses, students, physiotherapists, radiographers, &c.) to be told to identify themselves to patients and establish as good personal relations with them as possible. Ill people often cannot help seeming to be querulous and hypercritical.

2. Patients should at all times be kept "in the picture" as much as possible about their own progress. This could normally be the special responsibility of housemen. A patient should be told as early as possible after admission as much as he can take in regarding the nature of his illness, the treatment he will receive, and the length of time he is expected to have to remain in hospital. (This should not be interpreted, of course, as meaning that patients should be told of malignant disease or for that matter of slight hypertension and harmless cardiac murmurs.) The nature and possible consequences of any operation must be carefully explained (especially, for example, a colostomy or sterility). Many patients suffer needless worry through ignorance of the astonishing ease with which premedication and, say, intravenous thiopentone contrive to induce anæsthesia nowadays; they must be told in advance. Any changes in treatment and major investigations should be explained. Finally, before leaving hospital patients must always be given a practical summary of their diagnosis and prognosis.

3. It should be an invariable rule that for teaching of any kind, whether for a few minutes or an hour, the patient concerned must be warned in advance and his permission asked (it is almost always given in a good hospital), and afterwards, even more important, must be talked to (allaying any fears caused by misunderstood overhearing of the teaching) and thanked. The practice of many enlightened teachers of giving their larger teaching rounds in a small lecture-theatre, with patients (in bed or wheeled chair) brought in only for the necessary part of the discussion, should be more widespread.

4. Patients must be given ample opportunity *and encouragement* to ask questions and make complaints. A simple question such as "Is everything all right?" can make a considerable difference.

5. It is worth considering the idea of giving all patients and/or their relatives a small booklet on admission containing: (*a*) a general description of the hospital; (*b*) a brief outline of the functions and titles of the different medical and nursing staff, with spaces for insertion of the names of, say, the doctor in charge, houseman, ward sister, and anyone else whose name a patient might like to know; (*c*) a summary of the daily ward routine and time-table; (*d*) the correct postal address and times of delivery and collection of mail (which must of course be properly organised); (*e*) visiting-hours and any necessary restrictions of number and age of visitors; (*f*) outpatient and "casualty" hours and how and when to come to them; and (*g*) a cordial invitation to write to the hospital afterwards and make suggestions or complaints.

6. Some long-stay hospitals with a fair proportion of up-patients (such as tuberculosis hospitals) organise patients' committees concerned with, for example, meals, recreation, and general welfare. This idea should be extended and modified for all hospitals. In general hospitals dealing almost entirely with short-stay acute cases I suggest the formation of a patients' welfare committee, consisting of representatives of all branches of medical, nursing, and

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administrative staff, the hospital governors, local organisations (such as municipal or county councils), and—the important point—several ex-patients of all kinds. The function of this committee would be to advise the hospital governors on any points relating to patients' welfare in the broadest sense. Ex-patient members might be selected from personal knowledge by doctors or sisters and from any who have sent in good suggestions. It would be essential to include *recent* ex-patients.

Examples of the kind of suggestions such a committee would deal with are the following:

a. Meals should not only be well cooked but also well served, with good crockery and utensils (e.g., tea in cups *and saucers with spoons*).

b. Bed-lockers must be both sufficiently commodious and accessible from beds.

c. Extra baths, wash-basins, and lavatories are often needed, especially in surgical wards with modern ideas of early rising after operation.

d. Enough towels should be provided for all patients.

e. Reasonable dressing-gowns, pyjamas, and nightgowns, not looking like prison garments, should be provided for patients who do not bring their own.

f. Bed lights must have switches easily reached by patients lying in bed.

g. Visiting-hours should be adequate (I suggest at least 30 minutes every day—say 7.30 to 8 P.M.—as well as the usual hours and Saturday and Sunday afternoons).

h. Noise from all sources (e.g., floors, screens, trolleys, portable apparatus, electric motors) must be kept to the minimum, particularly at night. Many patients find that the only disadvantage of being in a large ward is being woken often during the night because of the attention neighbouring patients need. There should be sound and light proof cubicles in every ward, used only for the few patients who need attention at night, whether it be, say, three-hourly injections, supervision of intravenous therapy, or hourly gastric aspiration. With the addition of a few such cubicles I am in favour of large wards. Unless a patient can have many visitors at all hours of the day, he is much better off with many other patients (possibly including someone already recovering from the same complaint as his own) to whom he can talk.

i. Patients are woken at 5 A.M. in many hospitals because otherwise the night nurses cannot complete all their allotted tasks in time. If some of these tasks were handed over to the far more numerous day staff, half an hour's extra work before the ward is ready might give one or two extra hours' sleep to the patients.

j. The rule that patients must not get out of bed to go to the lavatory at night and during teaching hours is obsolete and unnecessary, also causing extra work for nurses.

I hope no-one at my own hospital will misinterpret this letter; personally I was exceedingly well looked after and I am very grateful to everyone who contributed to my rapid recovery. Some at least of the above suggestions may, however, help towards raising still further the already high standard of hospital care, and I will conclude with a reminder that appreciation is almost valueless if blind.

Cambridge. K. E. HALNAN.

PREFRONTAL LEUCOTOMY

SIR,—Prof. Alexander Kennedy commenced a series of wireless programmes with a balanced and useful contribution which was of much assistance to the cause of psychiatry. In a recent broadcast under the title of "The Frontal Lobes" he gave way to his medium by allowing the introduction of a degree of sensationalism into a programme which, if it should have been broadcast at all, ought to have been factual and accurate. The fact and accuracy in the portion of the programme on leucotomy related only to a particular type of operation, although generalisations were unfortunately made as if the term "leucotomy" had only this meaning. In fact the undesirable personality changes are exceptions rather than the rule following prefrontal leucotomy, and in this sense the term "prefrontal" is important.

In your issue of Jan. 15, Dr. Ström-Olsen and Dr. Tow again repeat this fallacy. Presumably their results condemn a type of surgical operation which has been the subject of criticism in the past and will, I hope, be regarded with still more disfavour in the future; but it would be unfortunate if, as their title suggests, leucotomy was generally thought to be represented by this archaic procedure. This can, however, be only surmise, as the type of operation is not defined in their article, the landmarks by which their incisions were made are not described, and about a third of the paper is given to elucidating the terms in which their results are expressed, which in the light of these observations can have no scientific accuracy for comparative purposes.

At the recent International Conference on Psychosurgery, at Lisbon, no less than eight widely differing operations were described under the heading of "leucotomy," but the definitions of the operations were such that the results had significance and the findings were of some value. It appears in fact that the article by Dr. Ström-Olsen and Dr. Tow really refers to late social results of extensive leucotomy operations (presumably performed, in some instances, by posterior section). Again if, as one supposes, the results were based on consecutive operations, the work apparently refers to the earliest cases performed at Runwell before experience of the procedure had been gained; if this is so, it is at least historically interesting.

In their conclusion they refute the justification of a "specific" indication for the operation; it should, however, be remembered that intractable pain is an "unequivocal indication." There is apparently some distinction made between "sane and well-preserved patients" and "chronic intractable obsessionals and depressive states." It seems regrettable, moreover, that a technique should after seven years be "so relatively crude"; one wonders if this means in comparison with other types of leucotomy operation.

Finally, other methods employing only limited incisions as used elsewhere give very satisfactory results in chosen cases without any of the gross signs of deterioration being found.

Netherne Hospital, Coulsdon, Surrey. E. CUNNINGHAM DAX.

STREAKINESS OF BLOOD FILMS

SIR,—In connexion with the preliminary communication under this heading a year ago,[1] I should like to call attention to the fact that I discussed the same phenomenon in a lecture delivered in November, 1936, and published in 1937.[2] I made the following points:

1. Whenever, with impeccable technique, blood films are streaky, provided that the patient is not grossly anæmic, the erythrocyte-sedimentation rate is raised.

2. The reverse is hardly ever true; very often a greatly increased sedimentation-rate is not associated with a streaky blood film.

3. Increased plasma-fibrinogen is a cause, though perhaps not the only cause.

4. Streakiness depends not on an increase in leucocytes but only on the nature of the disease process itself. I have observed the phenomenon when there were only slightly more than 8000 white cells per c.mm., whereas in a case of myelogenous leukæmia with 660,000 white cells per c.mm. the film was not streaky.

5. The change does not depend on temperature or moisture.

6. The disappearance of this change may herald the patient's recovery, even when the number of white cells has not yet decreased.

I also said that streakiness had up to then been observed in 5 groups of disorder: (1) all purulent or severe inflammatory pulmonary conditions; (2) all severe inflammatory liver and gall-bladder disorders; (3) malignant tumours of the liver associated with substantial intermittent fever; (4) subphrenic abscess with high fever; and (5) acute gonococcal epididymitis with high fever. Since then I have also observed the phenomenon in (6) purulent inflammatory diseases of the meninges and serous membranes. Thus in surgical disorders of the abdomen, such as appendicitis, cholecystitis, and salpingitis, streakiness is a danger-signal indicating immediate surgical intervention.

Finally, I should mention a case which stands by itself.

A female patient after an injection of serum for diphtheria of the throat developed very severe serum-sickness, with

1. Boveri, R. M., Waterfield, R. L., Newman, T. H. *Lancet*, 1947, ii, 831.
2. *Geneesk. Tijdschr. Ned.-Ind.* 1937, **77**, 393.

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pronounced fever and pronounced and painful swelling of the joints; the diphtheria itself was already clinically cured. The blood film was then fairly streaky. When, after about 5 days, the joints and the temperature returned to normal the streakiness was no longer detectable.

The Hague, Nov. 20, 1948. J. HAGA.

PENILE CARCINOMA AND CIRCUMCISION

SIR,—From your summary of the British Empire Cancer Campaign's annual report [1] it appears that according to Sir Ernest Kennaway, F.R.S., circumcision in Muslims is undertaken at the age of 14 years or later.

I cannot allow this statement to pass unchallenged. The majority of Muslims in India and in Pakistan are circumcised during the first month of life, and almost all Muslim children are circumcised by the age of 6 years. It is extremely rare to find a Muslim boy older than this who has not been circumcised. I think the same is true of other Muslim countries.

Department of Pharmacology, King Edward Medical College, Lahore, Pakistan. MAHBUB RABBANI.

AGRANULOCYTOSIS

SIR,—It seems that Dr. Black and Dr. Stanbury (Dec. 18) have paid too little attention to the main points in my article (Dec. 4). I should like to stress again that the most important measure in the treatment of agranulocytosis is the administration of penicillin in order to keep infection under control; with this there is often a tendency to spontaneous recovery, provided that the offending drug is discontinued.

This was demonstrated by the cases of Dr. Black and Dr. Stanbury and by my own, as is evident from an analysis of the figures and particularly the temperature charts. In each of the cases under discussion the temperature showed a definite downward tendency before the reappearance of granulocytes. Treatment with folic acid during this period of improvement did not contribute anything to recovery, which was already under way.

There is as little indication for giving folic acid as for giving pyridoxine; and the value of pentose nucleotides is doubtful.

Central Laboratory, Bulovka Hospital, Prague. J. H. WAELSCH.

INTRAVENOUS TREATMENT OF ANÆMIA WITH AN IRON-SUCROSE PREPARATION

SIR,—We should like to add some comment on our article in your issue of Jan. 1.

In the first place, our preparation was autoclaved at 15–16 lb. per sq. in., and not 115–116 lb. as wrongly stated in the text on p. 12. An important point in the whole process, given satisfactory reagents, is that the reaction is carried through with the minimal heating requisite for sterilisation. Under the conditions described, sucrose will just survive without significant breakdown. If the time of autoclaving is exceeded by even 5 minutes, or a higher pressure used, there will be caramelisation of the sugar; on completion the reagent should be cooled as soon as possible to room temperature.

In our anxiety to save space, brevity may have been carried to the point of obscurity. Knowledge of the properties of the disaccharides and of colloids was assumed, in those repeating our work, for close attention to detail in the preparation of this iron-sucrose complex is essential if breakdown of the sucrose is to be avoided. We wish to stress therefore the following points:

1. Analytical-grade reagents should be used, for though some "pure-grade" reagents may prove satisfactory, there is no certainty in this. It is especially important that the ferric chloride be anhydrous and free from hydroxy compounds or breakdown products, since it is very difficult if not impossible to reconvert them to the clear, negatively charged colloid phase.

2. The reagents must all be dissolved separately in water and added slowly, in the order given, on a water-bath short of boiling-point. Not more than a quarter-to-half the sucrose must be added until the alkali has been incorporated. If the sucrose concentration is too high in the early stages irreversible changes may occur, resulting in precipitation when autoclaved. These alterations are seen in the reaction mixture as a change from a clear red-brown colour to an opalescent, dirty greenish-brown colour.

Since June, 1948, a further 28 patients with iron-deficiency anæmia have been treated satisfactorily with a modification of the above preparation. The LD_{50} in mice of this new form is 8·6 ml. per kg. body-weight as against 7·4 ml. per kg. for the preparation described in the original paper. Clinically, it is much better tolerated than either our first preparation or 'Ferrivenin': it contains less unbound alkali and has a lower pH of 9·8–9·9 as against about 10·5. The results of this work will be submitted for publication in the near future.

May we end on a cautionary note? All these intravenous iron preparations are very irritant to the subcutaneous tissues and are only tolerated by the body to the extent that the plasma-proteins are able to "bind" the iron and the blood-stream able to dispose of the dissociating alkali. Recently several patients have attended our clinic, after having had from their own doctors considerable quantities of ferrivenin injected outside the antecubital veins, with resultant phlebitis, abscesses, and stiff elbows. It is admittedly not always easy to inject these dark-coloured solutions intravenously, and proof of being fairly in the vein must rest upon a free flow-back of blood into the syringe, which is in any case not undesirable as it helps to buffer the free alkali. The use of all these preparations should ordinarily be contra-indicated in patients who do not possess at least two easily palpable veins that can be used alternately.

Royal Infirmary, Manchester. H. G. B. SLACK, JOHN F. WILKINSON.

DOSAGE OF LIVER EXTRACTS

SIR,—The account by Dr. Mollin, in your issue of Dec. 11, of relapse in a case of pernicious anæmia during maintenance therapy with folic acid, raises the question of adequate initial and maintenance therapy in pernicious anæmia.

The case reported appears to be a typical example of the treatment with liver extract required in an average case. When it was decided to use liver extract ('Anahæmin') the average red-cell count was 2,900,000 per c.mm. Anahæmin 4 ml. fortnightly was given for 155 days (plus 20 mg. folic acid daily for the first 40 days). Only after this long period was a red-cell count of 4,900,000 per c.mm. achieved. This is to be expected, for the liver-extract dosage was just sufficiently above maintenance dosage to raise the blood levels. If 4 ml. weekly—or better, twice weekly—had been given, normal levels would probably have been restored in half this period.

It is simple to raise the level in a case of pernicious anæmia to 3–4 million red cells per c.mm., but it requires much more liver extract and a longer time to restore normal levels (4·5–5·0 million in females and 5·0–5·5 million in males with normal mean cell-volume). This fact is not stressed in textbooks or teaching, though Isaacs and his associates [1] have shown it to be so.

The treatment schemes recommended by various manufacturers of liver extract—1–2 ml. fortnightly in relapse—will not restore the blood level to normal in most cases of pernicious anæmia. The levels attained with this dose are usually about 3–4 million red cells per c.mm. This is the level at which the hæmatologist finds the average case of pernicious anæmia which is receiving supposedly adequate maintenance therapy. Unfortunately patients with such red-cell counts feel and look reasonably well; and the practitioner, in the absence of laboratory facilities, believes treatment to be adequate. These subnormal levels are an invitation to the development of subacute combined degeneration.

For maintenance therapy Dr. Mollin has treated the case reported with 2 ml. anahæmin fortnightly. This is the usual minimal maintenance dosage in large blood clinics—clinics with considerable experience of liver extracts. It is also the maintenance dose of commercial

1. *Lancet*, 1948, ii, 192.

1. Isaacs, R., Bethell, F. H., Riddle, M. C., Friedman, A. *J. Amer med. Ass.* 1938, 111, 2291.

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liver extracts which I find necessary for the great majority of cases of pernicious anæmia.

In view, therefore, of the frequency of inadequate therapy in pernicious anæmia in this country today, it is surely time that experienced hæmatologists made their views known on this matter, and that pharmaceutical firms revised their recommended dosage schedules in line with fact and not with commercial expediency. Too much liver extract cannot be given to a case of pernicious anæmia, and for treatment in general practice, where hæmatological control is usually impossible, minimal dosage should not be recommended.

In my experience, adequate treatment of the average case of pernicious anæmia requires at least 4 ml. weekly of any parenteral extract, until normal blood levels are restored—usually in 10–12 weeks. Thereafter a maintenance dose of 2 ml. fortnightly is required. If there is adequate evidence of successful maintenance treatment in pernicious anæmia with 1–2 ml. monthly of any available parenteral liver extract, I should like to be acquainted with it. Authoritative American opinion [2] appears to favour the view that very intensive treatment with 15 *U.S.P.* units liver extract should be given for at least a year before maintenance therapy is instituted!

Frodsham, Cheshire. J. G. A. MCSORLEY.

NO ROOM AT THE HOSPITAL

SIR,—The fact that THE LANCET has recently carried some timely criticism of thoughtless and impersonal treatment of patients in hospital encourages me to make some further observations on the vexed problem of hospital admissions, which since your leading article must now be very much in people's minds.

A short time ago I was in part responsible for the emergency admissions to a London teaching hospital. Daily I dealt, either directly or through the Emergency Bed Service, with general practitioners and the medical officers of other hospitals who were requesting admission for their patients: frequently I had to ask other hospitals to accept cases from our casualty departments when our beds were full.

Mr. Peers, in his letter of Dec. 25, indicates clearly that the admission of emergencies has recently become more difficult because the number of beds available has decreased. In the London area general practitioners and the E.B.S. find that patients who are elderly or whose stay in hospital is likely to be long are often not accepted for admission. Sometimes application has to be made to more than twenty hospitals—a time and temper consuming occupation. At many hospitals admissions are in the hands of junior house-officers who have little conception of, and even less sympathy for, a general practitioner's difficulties. Requests are sometimes met by unnecessarily abrupt and often rude refusals. In some hospitals porters seem to deal with admissions and refuse patients without any reference to their medical staff.

I know that beds are short and I agree with Lord Amulree that this problem must be solved by making more beds available, especially for the elderly. I know also that in teaching hospitals the admission officers have an added difficulty in that their beds are divided among a large number of staff, any one of whom may have only four or six beds for teaching purposes, and who is, not unnaturally, dissatisfied if an emergency admission turns out to be an elderly patient whose main need is not investigation or special treatment but merely good nursing care for a long time. But I feel strongly that hospitals are often unnecessarily tactless and thoughtless in dealing, either directly or through the E.B.S., with outside doctors.

Under the new National Health Act there is an unfortunate tendency to separate hospital services from general-practitioner services. Many of us can see a gulf beginning to form, and one of its causes is the lack of personal contact between hospitals and outside doctors. I believe that hospitals must take the initiative in preventing the appearance of this gulf. They could well start by ensuring that practitioners are dealt with promptly, politely, and helpfully when they request admission for emergency cases, and, if the admission must be refused, that the refusal does not leave the doctor with the impression that the hospital is not interested in helping him.

Those who deal with emergency admissions should remember that they are always dealing with sick patients and often with anxious practitioners.

Penarth, S. Wales. O. L. WADE.

NEW SURGICAL AND GYNÆCOLOGICAL FILMS

SIR,—In last week's annotation on this subject you say of one film that the colour effects are good "though the clear-cut image is absent, *as always in colour films.*"

This statement is completely inaccurate. Like many other ciné enthusiasts I now use colour exclusively, because of its beauty, and, like my fellow devotees, can show you thousands of feet of film with the image so clear and the stereoscopic effect so marked that you would almost feel you were looking at the original subject. I can show you shots taken at only 8 in. from the object—e.g., a small tumour $^1/_2$ in. in size being dissected by scalpel and forceps, where the scalpel blade fills half the screen yet all the outlines and details are perfectly clear and sharp. Even the copies of such films show no blurring.

Colour films with fuzzy images are due to several causes. I make no attempt to place them in any order other than that of convenience.

1. Poor or careless focusing. One has to be meticulous about this. It is the usual cause of my failures.
2. Insufficiently powerful lighting, so that a wide aperture is required. I personally aim to light the subject sufficiently to allow apertures of f 5·6 and occasionally f 4.
3. A lens which has a "soft focus." I am just replacing one of mine for that reason.
4. 16 mm. "copies" of 35 mm. film. The reason is poor technique.
5. A defective camera or lens. They are not all perfect.

No, Sir, you must retract your statement.

Manchester. W. SAYLE CREER.

THYMIDINE AND VITAMIN B_{12} IN PERNICIOUS ANÆMIA

SIR,—Microbiological methods have shown that liver extracts effective in pernicious anæmia may contain, besides vitamin B_{12}, certain functionally related substances. Of these, thymidine (thymosine or thymine desoxyriboside) was isolated from liver as a factor preventing the toxicity of "methyl folic acid"—a competitive antagonist of folic acid.[1]

It was then discovered that thymidine would replace vitamin B_{12} in the nutrition of certain lactobacilli.[2,3] Wright and his co-workers[3] believe that vitamin B_{12} functions as a co-enzyme concerned with converting thymine to thymidine. They suggest that the primary biochemical defect in pernicious anæmia may well be inability to synthesise certain nucleosides, particularly thymidine, from parent purines or pyrimidines. According to their theory the hæmatopoietic effect of folic acid in this disease arises from increased thymine synthesis,[4] which by mass-action effects yields more thymidine. They explain the effectiveness of large amounts of thymine in pernicious anæmia[5] on a similar basis.

This microbiological evidence suggested a trial of thymidine in pernicious anæmia. The pure substance is very scarce, but after a wide search a small quantity was obtained through the generosity of Dr. Thomas G. Brady, of the department of biochemistry and pharmacology, University College, Dublin.

Realising that the material, even if clinically active, might prove to be effective only in large doses, we gave the entire quantity (48 mg.) to one patient, a woman,

2. Haden, R., Bortz, D. W. *Ibid*, 1948, **138**, 870.

1. Shive, W., Eakin, R. E., Harding, W. M., Ravel, J. M., Sutherland, J. E. *J. Amer. chem. Soc.* 1948, **70**, 2299.
2. Shive, W., Ravel, J. M., Eakin, R. E. *Ibid*, p. 2614. Snell, E. E., Kitay, E., McNutt, W. S. *J. biol. Chem.* 1948, **175**, 473.
3. Wright, L. D., Skeggs, H. R., Huff, J. W. *J. biol. Chem.* 1948, **175**, 475.
4. Stokes, J. L. *J. Bact.* 1944, **47**, 433.
5. Spies, T. D., Vilter, C. F., Cline, J. K., Frommeyer, W. B. jun. *Sth. med. J.* 1946, **39**, 269.

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aged 72, with classical addisonian pernicious anæmia in relapse.

During a control period of 14 days reticulocytes did not exceed 0·8% and the red blood-cell count fell to 2,360,000 per c.mm. (hæmoglobin 9·5 g. per 100 ml., mean corpuscular volume 114 c.μ, mean corpuscular hæmoglobin concentration 35·1%.) Marrow puncture showed megaloblastic erythropoiesis. Gastric achlorhydria persisted after histamine and alcohol.

The thymidine was given intramuscularly in divided doses over a period of 2 hours with no untoward reactions. There was neither clinical nor hæmatological improvement. Reticulocytes did not exceed 1·8%, and after 10 days the bone-marrow was still megaloblastic.

This complete failure to respond to thymidine could not have been due to "resistance" on the part of the patient, since she now responded well to a small dose of a known potent material—namely, 7·5 μg. of a red crystalline anti-pernicious-anæmia factor[6] which is either identical with, or closely allied to, the vitamin B_{12} of Rickes and his associates.[7] Reticulocytes rose on the 4th day, reaching a peak of 3·8% on the 6th day; clinical improvement was evident, and by the 15th day the red blood-cell count had risen from 2,330,000 to 3,220,000.

Although the reticulocytosis was submaximal the increase of red blood-cells in 15 days (890,000 per c.mm.) compared well with the expected response from similar initial red blood-cell levels, according to both the "average" formula of Della Vida and Dyke[8] for parenteral liver therapy (920,000) and our unpublished formula based on responses to red crystalline material in higher dosage than used in this instance (910,000).

Thus thymidine, which can replace vitamin B_{12} in the nutrition of certain bacteria, has proved ineffective in pernicious anæmia, at least in this case and in the dosage given.

Royal Victoria Infirmary, Newcastle-upon-Tyne. C. C. UNGLEY.

HOSPITAL BIOCHEMISTS

SIR,—I suggest that your correspondents, "Ph.D." and "Clinical Biochemist," are arguing about names rather than functions to be carried out by an individual. The "hospital biochemist" in the routine laboratory must be a reasonably competent chemist, but his functions are: (1) to maintain the accuracy of well-standardised procedures; (2) to select suitable new methods for adoption; and (3) to act as a consultant and to undertake clinical research. The routine laboratory is not a suitable place in which to conduct fundamental chemical research.

These functions do not require a man highly trained in chemistry; the more abstruse branches of kinetic theory, or of thermodynamics, are not needed: a good general knowledge of descriptive chemistry, some knowledge of physical chemistry, and a wide knowledge of human physiology and of some branches of analytical chemistry would suffice. I need hardly point out that all medical graduates study chemistry to about the standard required for a general B.SC.

The chemist has received a fundamental training in which physical chemistry plays a large part, while analytical chemistry receives very little attention, and human physiology is almost completely neglected, unless special courses are attended. I well recollect the hard study I undertook when, as a non-medical chemist, I entered the clinical laboratory at St. Bartholomew's Hospital; it was nearly a year before I was any use to the department.

I submit that for routine laboratories the advantages of a medical graduate outweigh the disadvantages encountered when he is not chemically qualified. For research laboratories there is little doubt that the reverse is true; and broadly speaking, professors are expected to undertake research, not routine work.

Finally, it is an error to suppose that senior hospital appointments will be given to anyone 3 years after qualification. A more reasonable estimate would be 2 years' clinical work, followed by 4 years in the laboratory with approximately registrar status, and 2–5 years as a senior assistant—a total of 12–16 years from entering the university or medical school. The medically trained man attains these senior positions at ages between 32 and 40—not earlier. If "Ph.D." expects to receive a senior hospital appointment at the age of 26, he is indeed an optimist.

Central Middlesex Hospital, London, N.W.10. GEORGE DISCOMBE.

6. Smith, E. L. *Nature, Lond.* 1948, **161**, 638; *Biochem. J.* 1948, **43**, 8.
7. Rickes, E. L., Brink, N. G., Koniuszy, F. R., Wood, T. R., Folkers, K. *Science*, 1948, **107**, 396.
8. Della Vida, B. L., Dyke, S. C. *Lancet*, 1942, ii, 275.

A WALKING-CHAIR FOR SPASTIC CHILDREN

SIR,—The letters from Dr. Dunham and Mrs. Collis in your issue of Dec. 11 very rightly stress that in cerebral palsy the first and most important part of therapy is thorough movement training. Without this training, faults of posture and coördination perpetuate themselves.

The device I described was intended as an adjunct to this régime. When the spastic child first bears weight his muscles are subject to unaccustomed stress and their patiently acquired control is often inadequate. If this stress can be reduced by the suspension device, full control is possible. As muscular control becomes sufficient to deal with increased stress the "lift" can be reduced, and when control is adequate with full weight-bearing the machine is discarded. Thus apart from palliative use in the severest cases the machine should only be used in the first month or two of weight-bearing exercises.

I should like to emphasise that machinery can provide no short cuts in treating spastics. In no condition is more patience demanded of the teacher and the taught; fortunately the reward of this patience is great.

Darlington. PHILIP WRIGHTSON.

NURSING EXPERIENCE FOR MEDICAL STUDENTS

SIR,—The differences of opinion expressed in your correspondence columns on the suggestion to give medical students a short course in practical nursing recalls the period of three months when I was a clinical clerk to Dr. Samuel West at St. Bartholomew's Hospital.

I was fortunate enough to have rooms in the old residential part of the hospital, where some twelve students lived; so I was "available" night and day. The sister of the men's ward, who was a bit of a tyrant in some ways, got two of us to attend in her ward when needed, and she taught us how to nurse. We had three or four cases of typhoid fever and some pneumonia at the time, and we had to turn out when called and attend to them.

Under the supervision of sister I learned how to change the bed of a severely ill patient with typhoid who had got a "dirty bed." I learned the right way to lift a patient, how to make a linseed poultice for lobar pneumonia and get it on hot, how to keep temperature charts neatly, and many other small but important details of nursing. I remember how I hated it all at the time; but now, some 35 years later, I am grateful to that sister. As a G.P. I have had many an opportunity of applying her teaching to the benefit of a patient.

In my early days, I remember, I was called to see an old woman on my panel list who was lying in a dirty bed with the clothes all tumbled about. I set to work and remade that bed and made the patient comfortable, but her attitude was far from grateful. It was not a doctor's job to make beds. During the past 28 years I have been an officer in the St. John Ambulance Brigade and have given many courses of instruction in first-aid and also in home nursing as well as judging competitions which involved putting an injured person to bed; and I feel I could not have judged fairly without the knowledge I had gained. I do not profess to be a "trained nurse," but am sure I have been a better family doctor owing to that early training.

It may well be that in these more advanced times a G.P. is too busy to spend a little time in bed-making or showing the relatives how to make a patient really comfortable, but I can assure anyone who cares to undergo a short training that he will be amply rewarded. Times have changed and the syllabus is grievously overloaded with items which must be studied in order to satisfy examiners. Yet one cannot help noticing that

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the young men today lack knowledge of those small but important niceties of practice which help the sick so much.

Now that psychiatry and psychotherapy are all the rage it seems to be forgotten that much of the "bedside manner" was, and still is, based on them, and that making a sick person comfortable in body is half way to making him mentally so.

Bournemouth. CHARLES MORSE.

SIR,—If, by the time a medical student reaches the final year, his powers of observation are so poor that three and a half years' attendance (and probably some periods of residence) in the wards and hospital have not shown him the fundamentals of nursing practice without recourse to a three weeks' special instruction, then I do not believe that he is a fit person to practise medicine in the world outside, where, so my teachers say, the observations of the general practitioner are the first step in the elimination of disease.

Medical School, Birmingham, 15. JAMES R. CROSS.

SIR,—The opinions expressed by Mr. Carruthers and Mr. Richardson in your issue of Jan. 8 have been rightly condemned in your editorial comment. In the introductory course which a student of this hospital attends after completing the preclinical part of his training, a short course in practical nursing has been included for the past nine months. On the whole the students of this hospital have liked it, and a number have suggested that more time should be devoted to it.

D. HANBURY.

Department of Medicine, Middlesex Hospital, London, W.1.

CRASH HELMETS

SIR,—Letters I wrote to a lay paper on the use of crash helmets by motor cyclists, has brought the following points to light:

1. The motor cyclist is completely indifferent to the value of a helmet; each is sure that he or she will never be involved in an accident. If hunting people wear bowlers and "toppers" against falls, surely it is not too much to expect the cyclist to wear a helmet.

2. No-one knows who stocks helmets; and I have been unable to discover any shop or garage which keeps them.

3. The pattern used by "dirt-track" riders is far too expensive, costing £6–9; and it is uncomfortably hot and heavy.

4. It is impossible to make the crash helmet compulsory. Mr. David Eccles, M.P., points out that if—as happens—workers in certain dusty industries disregard masks the wearing of which is supposed to be compulsory, it would be even more difficult to enforce the use of these helmets by law.

5. The Automobile Association is "not convinced that the compulsory use of the crash helmet is necessary in the interests of road safety."

6. The only possibility of enforcing the use of the crash helmet lies with the insurance companies, which could refuse to pay for injuries sustained through non-usage of the helmet; they are not very keen on insuring motor cycles at the best of times.

Sir Hugh Cairns has stated that 85% of all fatal motor-cycle accidents involve the skull and/or brain. These figures are serious enough to warrant these helmets. A large number of motor cyclists are between the ages of 16 and 25—men and women who are just becoming useful members of society. The motor cycle, probably more than any other means of locomotion save flying, gives the impression of infinite power; it behoves us to save these young people from their foolhardiness.

Through the kindness of Mr. H. Duff, of the Army Recruiting Office, I examined the ordinary Army crash helmet, which he assures me has saved many a man's life. It is made of papier mâché; inside are pieces of webbing which rest on the head, a wide space separating the skull from the helmet. Round the edge is pleated crêpe rubber, again separating helmet from head. Mr. Duff says that the weight is not noticed up to 2 hours; after a long day's riding, however, it feels heavy and headache tends to develop. Once popularised, the helmet should sell at about 15*s*.

Maxwelltown, Dumfries. A. P. BERTWISTLE.

OSTEOPATHY

SIR,—I should like to associate myself with the suggestion implied by Batchelor and Cohen, in their report of Dec. 25, that manipulation should form part of the normal treatment carried out at any hospital. The fact that the words used by osteopaths to describe their concept of the lesion are not those used by orthodox medical men does not invalidate the modicum of truth in osteopaths' claims—namely, that manipulation of a spinal joint is sometimes a useful therapeutic measure. The results of treatment impress patients more than the scientific accuracy of diagnosis, and many a manipulation by an osteopath, based though it often is on the mistaken supposition that a bone is out of place, has abolished long-standing pain.

For the past ten years it has been my hope and endeavour that physiotherapists should be taught manipulation of joints, thereby eliminating the need for lay manipulators. Dr. J. B. Mennell taught manipulation to the physiotherapy students at St. Thomas's Hospital before the war, and I have continued similar tuition ever since. It is my view that any patient cured by a manipulation by an osteopath should have been cured by the same manipulation given by a physiotherapist [1] or a medical man. To this end, weekly demonstrations are given in our department to medical students, and practical classes form part of the routine work of the physiotherapy students.

One of the A.M.O.'s now working in this department took the postgraduate course for medical men at the London College of Osteopathy, and it is clear from his opinions and his technique that a satisfactory level is attained. Many of the methods taught to him are very similar to my own, but osteopaths appear sadly to neglect strong traction as an important adjuvant to manipulations calculated to reduce intra-articular displacements, especially at the spinal joints and knee. Traction increases effectiveness and safety, thus facilitating undergraduate instruction. I believe that some of osteopaths' methods have been considerably improved upon.[2]

The institution of our health service has drawn urgent attention to this problem [3]; for the State has now assumed responsibility for all medical care. Thus a doctor may well order manipulative treatment for a number of common conditions (e.g., tennis-elbow [4] or a displaced fragment of intervertebral disc [5]) only to find that there is no medical auxiliary in his district acquainted with the proper techniques. This situation plays the medical and physiotherapy professions into the hands of lay manipulators, many of whom are now forming themselves into associations expressly to obtain State recognition.

Clearly manipulators—most of them self-styled—fill an important gap in medical treatment, which the London College of Osteopathy is laudably helping ethically to close. But at the present rate it will take centuries to replace the 3000 or so laymen concerned. The dilemma for the State, and the present threat to patients' welfare and purse, would be quickly resolved if physiotherapy students were all taught manipulative technique as a matter of course. In this simple way persons of varied skill and competence could be quickly replaced by properly qualified medical auxiliaries.

JAMES CYRIAX
Physician to the Department of Physical Medicine.

St. Thomas's Hospital, London, S.E.1.

SIR,—May I comment briefly on the letter which you published on Jan. 8 from the editor of the *Osteopathic Quarterly*?

The London College deviates from ordinary osteopathic educational standards in that instruction is confined to a postgraduate course for registered medical men, working on the assumption that it is neither necessary nor feasible to teach all the basic subjects to a student who has already passed these subjects in a recognised

1. Cyriax, J. *Physiotherapy J.* 1947, Jan., p. 102.
2. Cyriax J. Deep Massage and Manipulation Illustrated. 4th ed., London, 1948.
3. Cyriax, J. *Brit. med. J.* 1948, i, 362.
4. Mills, G. P. *Ibid*, 1928, i, 12.
5. Cyriax, J. *Lancet*, 1945, ii, 427.

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medical institution. The only exception to this is where the application of the osteopathic principle may necessitate greater clarification beyond ordinary medical teaching. The curriculum clearly covers all subjects thought necessary to give the medical graduate a complete knowledge of osteopathy. The teaching staff has been principally those practitioners, medically qualified and otherwise, who are in practice in London and the near provinces. It is admitted that all instruction can be improved, and it will be improved in the near future.

In view of the educational standard of the college, it is not expected or desired that it should be recognised by the Council and Register of Osteopaths.

The American Osteopathic Association definitely recognise and appreciate that the London College has established a new principle, admittedly experimental, in osteopathic education, which must be tried out and developed before recognition by the American Osteopathic Association can be granted. The desire of the British Osteopathic Association in sponsoring the college is to see osteopathy an integral part of general medical education and practice, and it is felt that the present method is a sure way to this end. The main object of members of the British Osteopathic Association in supporting the college is the desire for the future expansion of osteopathy, with all its benefits to humanity.

In conclusion, I would like to point out that it is not correct to say that the college only possesses one student.

London College of Osteopathy, N.W.1. — A. F. LOCKWOOD, Secretary.

SIR,—I must reply to your comment on my letter published last week.

I have been interested in osteopathy for more than 16 years and have not only read textbooks on the subject but also have seen osteopaths with various kinds of qualifications at their work. Their claims as to special skill at manipulation are as fantastic and as unsubstantiated as is the theory of osteopathy. They claim that the basis of the manipulation of the spine is what they call "isolation of the vertebræ," and that, just as a man can take each of his fingers in turn and pull and twist them, so they can isolate a vertebra and lift it up, twist it, turn it and push it back into place. Hugh Owen Thomas and others long ago exploded the idea of magical fingers feeling lesions which nobody else can feel and doing manipulations which are completely divorced from what we know of anatomy and physiology.

But, Sir, my quarrel with you is not so much over the truth or otherwise of the rubbish of the osteopaths, but with your encouragement of their ridiculous claims; for the word will go forth that THE LANCET on Dec. 25, 1948, wrote in a leader: "'About things on which the public thinks long,' said Samuel Johnson, 'it commonly attains to think right.' And we have to accept the fact that public opinion has come to lean on osteopaths for several types of treatment; that kings, nobles, and the common people patronise them;" and also "The new college [of osteopathy] can be regarded as a creditable attempt to organise and evaluate osteopathic ideas, and to curb the opportunist or the quack, and to this extent the enterprise appears commendable." You also ask that osteopaths be called in to train orthopædic surgeons in special osteopathic manipulations. Do you realise that every osteopath will now be able to claim—and they will not be slow or quiet in their claims—that the orthopædic surgeons of the country, being unable to treat their patients properly, have been forced at last to call in the help of the osteopaths. I feel certain that when you commissioned Batchelor and Cohen, and when you wrote your leader, you must not have realised the implications of your act.

Any medical man who reads textbooks on osteopathy must realise the worthless nature of the osteopaths' claims, their ridiculous ideas on ætiology and pathology, and their danger to all patients who are unfortunate enough to come in contact with them. Any medical man must therefore view with grave suspicion, to say the least, the intelligence or motives of any qualified medical man who takes up osteopathy. To have any truck with osteopaths is to endanger the good repute of the medical profession.

Perhaps the final word on osteopathy was said by a Sheffield unqualified practitioner, who had under his name on his plate: "Osteopath, Naturopath, Psychopath."

SIDNEY PAPPWORTH.

Orthopædic and Accident Dept., City General Hospital, Sheffield.

REGIONAL REPRESENTATION ON THE JOINT TUBERCULOSIS COUNCIL

SIR,—The letter from Dr. Gray in your issue of Jan. 1 criticises the Joint Tuberculosis Council for (*a*) postponing any decision with regard to regional representation on its council for a period of six months, (*b*) refusing representation to the newly founded Liverpool Regional Tuberculosis Society, and (*c*) having an unrepresentative constitution.

By the council's constitution all existing clinical tuberculosis associations and societies are represented, the only exceptions being those associations having limited constitutions—e.g., areas of membership limited by local-authority boundaries. The council's interests are wide and are not limited to terms and conditions of service; in fact these in the past have comprised only a small fraction of the council's work. It is not necessary to detail the subjects considered by the council as these are faithfully reported in your journal from time to time.

Rule 5 of the constitution restricts the size of the council; a large deliberating body would be unwieldy and would make it impossible to conduct business in the limited time available for meetings. To avoid delay, Liverpool members of the North-West Tuberculosis Society should put their views forward to that body, whose representatives could then bring them before the Joint Tuberculosis Council. This is the constitutional and most rapid and effective way of proceeding.

It was foreseen that regional groupings would probably result in the formation of new clinical societies and that these societies would seek membership of the council. There is ample time for the new societies to show their worth before any question of displacement of the old and tried clinical associations in favour of the new bodies is considered.

It is appreciated that the Joint Tuberculosis Council is not primarily constituted to consider terms and conditions of service. The only reason that the council is taking an active part in work of this nature at the present time is the absence of representation of tuberculosis workers on the Central Consultant and Specialists Committee and the lack of an alternative avenue of approach other than through the tuberculosis group of the Society of Medical Officers of Health. This latter body is better constituted to deal with such matters as terms of service, but joint action is taking place at the moment to ensure full support for the representations to be made.

D. P. SUTHERLAND, Chairman.
Joint Tuberculosis Council, Oxford. — N. J. ENGLAND, Hon. Secretary.

RADIO TRANSMISSION OF ELECTRO-PHYSIOLOGICAL PROCESSES

SIR,—At this hospital we have for some time been carrying out experimental radio transmission of the electro-encephalogram and electrocardiogram. We feel it would be of interest to describe briefly what is in progress at our centre, particularly because many may see applications to their own problems of the ideas we have in mind, and it would help us to know the scope of such possible applications.

Since September, 1947, when a licence was obtained from the Post Office, we have carried out numerous radio transmissions of electrophysiological processes of the body—particularly the electro-encephalogram and electrocardiogram. The encephalogram or cardiogram is radio-transmitted direct from the patient to another part of the hospital where it is received and recorded. We are now experimenting with portable transmission, to see whether the encephalogram or cardiogram can be

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transmitted from the subject while he goes about his normal, or specially selected, activities. Clearly such ambulatory transmission would offer openings for further physiological studies.

In discussing this subject with others we have found that the question of telepathy is usually raised. On theoretical grounds there is no justification for believing that radio transmission of the electro-encephalogram is likely to assist telepathy. Nevertheless, some will probably wish to repeat previous telepathic experiments with the subjects transmitting their electro-encephalograms to each other during the experiments.

C. C. BREAKELL
Whittingham Hospital, near Preston. C. S. PARKER.

Public Health

Influenza

DEATHS certified as due to influenza in the 126 great towns of England and Wales rose to 47 in the week ended Jan. 8, compared with 29 in the previous week. This rise is not disproportionate for the season and suggests that virus influenza had not reached epidemic proportions.

Spread in Europe.—Influenza has spread across Europe from the south-east. The disease appeared in Italy early in December and had crossed to the Haute-Savoie by about Dec. 15. It spread up the eastern border of France between the 15th and the 20th, and jumped to most of the country sparing only a few departments. It seems that it was not present until about the 20th in Paris, where the attack-rate became appreciable about Christmas; here it took about a fortnight for the disease to reach a maximum, where it has remained. There is so far no sign of regression. A conservative estimate of incidence in the population of France up to the present is 15%. Some communities have experienced attack-rates up to 30% or even 40%.

The spread to the northern European countries continues. In Holland the disease entered Eindhoven on Dec. 31, and it appeared in Leyden a week later. Outside France and Italy, according to telegraphic reports received in Geneva up to Jan. 11, there had been no abnormal influenza increase in Scandinavia, Spain, Hungary, or the American Zone of Germany. The disease was prevalent in the Vorarlberg Tyrol of Austria. In Switzerland 13 cantons were affected, particularly Tessin, Geneva, and Basle. To the east there were small foci in certain towns in Turkey but no epidemic. In northern Europe the epidemic was still confined to south Holland.

Clinical Features.—The disease in France is typical influenza, easily distinguished from the benign seasonal catarrhs. The average case begins abruptly with headache, weakness, muscle pains, and fever. Apart from a little sore throat, signs referable to the respiratory system are few at onset. In the average case the illness lasts a week, followed by some debility which may extend convalescence. Complications are few and encephalitis has not been reported. Secondary pulmonary complications have killed elderly people. A few deaths from acute pulmonary œdema in the first thirty-six hours of the illness, particularly in children under 2, have been mentioned.

Virology.—In a previous announcement virus B was mentioned. It now seems more probable that the virus mainly responsible is more closely related to type A. Identification experiments at the World Influenza Centre laboratory at Hampstead are incomplete.

Diphtheria in 1948

In England and Wales diphtheria mortality last year was the lowest on record. In the 126 great towns, which cover about half the population, deaths numbered 100. Notifications totalled 5182—also a new low record. In 1941, the year in which the immunisation campaign got under way, deaths and notifications in the great towns numbered 1487 and 27,613 respectively.

Food-poisoning from Lamb's Tongue

An account of food-poisoning affecting 50 of 1072 people who ate lamb's tongue in a factory canteen has been given by Miss Betty Hobbs, PH.D., and Dr. Mair Thomas.[1] Those affected had acute vomiting and diarrhœa accompanied by abdominal pain, weakness, and, in extreme cases, shock and collapse.

The tongues had been received frozen in sacks. Soon after receipt they were removed, washed, and allowed to thaw. They were then boiled for $2^1/_2$ hours, spread out on trays, and, when sufficiently cool, skinned by hand. The skinned tongues remained spread out on trays for a further 2–3 hours until cool enough to be placed uncovered in the cold-room. The next morning the tongues were removed and sliced by one member of the staff, who held them by hand. The slices were put on to cold plates, vegetables were added, and each plate was put into the hot-plate container; the gas in the container was lit an hour before the meal, the temperature in various parts of the container ranging from 42 to 160°C.

From tongues which had been left over were isolated coagulase-positive staphylococci type III (c), phage-type 42D. Two persistent hand carriers and one intermittent nose carrier of the infecting staphylococcus were found among the kitchen staff who had helped to skin the tongues; and this staphylococcus was frequently isolated in large numbers from cuts and abrasions on the skin of the two hand carriers. The same organism was found also on table tops and in floor dust. The authors conclude:

> "The outbreak was due to faulty handling of a meat product cooked the day before it was intended to be eaten. These errors in food-handling are usually made in ignorance, and it is possible that they could be prevented by teaching food handlers the elementary requirements of good food hygiene."

Obituary

ALEXANDER BROWN JAMIESON

M.B. EDIN.

Dr. A. B. Jamieson who, since 1919, was a member of the tuberculosis medical staff of the Lancashire county council, died at his home at Great Eccleston, on Dec. 16 last. He received his medical education at the University of Edinburgh, where he graduated M.B. in 1910. After joining the staff of the council as an assistant T.O., he worked in the districts served by dispensaries at Eccles, Leigh, Stretford, Farnworth, and Pendlebury, and also at the Peel Hall Pulmonary Hospital, Little Hulton. In 1945 he was appointed a member of the senior staff and became the medical superintendent of the Elswick Sanatorium, near Kirkham, and consultant tuberculosis officer for the Fylde dispensary area. When the Manchester Regional Hospital Board established an enlarged dispensary area bringing in Blackpool county borough, Dr. Jamieson also became the chest physician of the Victoria Hospital in that town. He leaves a widow and one son.

Mr. S. F. A. COWELL, for many years secretary of the Royal College of Surgeons of England, died at St. Albans on Jan. 13 at the age of 85. The son of Dr. T. W. Cowell, he was educated at Westminster School and University College, Oxford. Soon after taking his B.A. degree in 1886, he joined the staff of the college as assistant secretary, a post which he held till in 1901 he succeeded Edward Trimmer as secretary. He retired in 1934. The college and its welfare was the centre of his whole life, and as a loyal and conscientious official he took care to husband its resources and to safeguard its position. His work was done with charm and kindliness which will be gratefully remembered by many.

The death is announced of Dr. C. F. GOOD, C.B., of the Ministry of Health, the principal medical officer in charge of the insurance medical service.

1. Hobbs, B. C., Thomas, M. E. M. *Mon. Bull. Min. Hlth. P.H.L.S.* 1948, 7, 261.

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Notes and News

CLASSIFIED ADVERTISEMENTS

THE number of medical appointments advertised at the end of THE LANCET is rising; and it is more than ever necessary that advertisements should be classified so that the reader can quickly find those that interest him. In and after our issue of Feb. 5 we shall group short advertisements under the following headings:

1. Academic and Educational.
2. Hospital Services: Senior Appointments.
3. Hospital Services: Junior Appointments.
4. Public Appointments.
5. General Practice.
6. Appointments: Too late for Classification
7. Miscellaneous.

The two sections covering hospital appointments will have groups for London and Provinces, and the appointments will, normally, appear under the name of the hospital at which they are to be held. This will sometimes necessitate small changes in the form in which the advertisement is submitted; but the advantages of an intelligible scheme are such that we hope these changes will be tolerated. Any form of classification presents practical difficulties, and none can be wholly logical. But we hope that, with or without later modification, the system now to be introduced will commend itself both to advertisers and readers. We ask for their forbearance at first.

PRECOCTIC

IN the paper on macrocytic anæmia in relation to ancylostomiasis, which we published last week, Dr. H. Lehmann sought to introduce the term "precoctic" to describe cells emitted from the bone-marrow before they are fully ripened (*coctus* = ripened or cooked). His intention was defeated by an unfortunate mischance which led to the word appearing, throughout his article, as "coctic." We much regret this mistake, which must have confused readers. It originated in a discussion whether "pre-" was the prefix that would best convey Dr. Lehmann's meaning: by analogy with "precocious," similarly derived, it might perhaps be held to imply that the cell was already fully matured. Dr. Lehmann decided that "precoctic" was on the whole preferable to "antecoctic," or the hybrid "acoctic," which were possible alternatives, and we intended to convey this decision to our printers. Only through a series of accidents did the word appear without any prefix at all.

Dr. Lehmann's paragraph introducing the word should have read as follows:

> The reticulocytes and cells in the early postreticulocytic stage are here called precoctic cells. By precoctic blood picture is meant one due to a condition where large cells are produced in regeneration, the macrocytosis not being due to a disturbance of bone-marrow function by the absence of essential nutrients but being, on the contrary, caused by a hyperactivity of the marrow which leads to an emission of slightly "unfinished" cells (*coctus* = fully mellowed). To call these cells immature might suggest an inhibition of cell production at the nucleated stage, and the term "regenerative" would not differentiate from a state where regeneration proceeds without macrocytosis.

JOURNAL OF PHARMACY AND PHARMACOLOGY

THE Pharmaceutical Society's *Quarterly Journal of Pharmacy and Pharmacology*, which came into being in 1928 as the successor to the Yearbook of Pharmacy, has now been replaced by a monthly, the *Journal of Pharmacy and Pharmacology*, edited by Dr. C. H. Hampshire. The new journal, of which the first issue appeared this month, is obtainable, at a cost of £2 per annum or 5*s*. for a single copy, from 33, Bedford Place, London, W.C.1.

University of Oxford

On Dec. 16 the following degrees were conferred:

D.M.—A. E. Mourant.
B.M.—H. E. Reiss, D. F. Mullins, M. H. Hall, Joan W. Kipling,* Janet E. McKinstry.*

* In absentia.

Royal College of Physicians of London

Dr. Marc Daniels will deliver the Milroy lectures on Tuesday and Thursday, Feb. 15 and 17, at 5 P.M., at the college, Pall Mall East, S.W.1. He is to speak on Tuberculosis in Post-war Europe.

University of Glasgow

On Jan. 15 the following degrees were conferred:

M.D.—G. C. Arnell, K. C. Hutchin, A. W. Lees, George Leslie, J. S. Stevenson.

M.B., Ch.B.—A. H. Alexander, C. I. S. Bartlett, Mary P. S. Borland, Lucy McL. C. Boyd, Mary B. S. Calder, Adam Carnochan, Mary E. Catto, Agnes A. Coughtrie, R. McL. Douglas, W. I. L. Fraser, G. L. Gibson, D. A. Haldane, Mary M. Hamilton, A. C. Howie, A. N. Hunter, Bernard Joels, Elizabeth M. S. Kilpatrick, Anne K. Kirkland, D. A. Knox, R. R. Lang, D. McC. Macgregor, John MacKay, A. M. Mechie, A. P. Miller, A. R. Morrison, John Morton, J. J. Mullen, P. R. Probert, J. D. Read, H. A. Roemmele, Leslie Rose, Christina C. Stevenson, I. O. Stewart, James Stewart, J. A. M. Stewart, R. E. Stewart, W. S. Stoddart, Peter Stuart, H. W. Thomas, D. B. Turnbull, J. M. Uku, James Wright.

Royal College of Surgeons of England

At a meeting of the council held on Jan. 13, with Lord Webb-Johnson, the president, in the chair, Prof. J. R. Learmonth was admitted to the honorary fellowship. Mr. J. E. Piercy (London), Prof. V. F. Lambert (Manchester), Mr. Norman Hodgson (Newcastle-on-Tyne), and Mr. G. H. Buckley (Blackpool), being fellows of the Royal College of Surgeons of Edinburgh, were elected ad eundem to the fellowship.

A diploma of fellowship was granted to A. G. Jessiman, and of membership to D. N. H. Owen and I. S. Waller. The following diplomas were granted jointly with the Royal College of Physicians:

D.L.O.—G. G. Allan, M. D. Cremin, K. H. Dalrymple, P. G. Jay, Parimal Kumar Khasnobis, R. M. Lang, H. A. J. Lister, Ilija Lopert, W. R. McKechnie, V. St. J. de C. Magian, W. H. Mirkin, Constance B. S. Napier, Man Mohan Nath, S. S. Ovanessoff, W. M. Owen, R. E. Peasegood, Aubrey Schiller, Ching Tuan T'ang, R. H. Welch, T. J. Wilmot, I. S. Young.

D.I.H.—William Blood, L. B. Bourne, J. A. Harrington, A. K. Hill, W. T. W. Lawson, R. F. L. Logan, A. C. Mackay, George Milne, J. G. Mott, Haridas Mukhopadhyay, A. J. Patterson, Joti Ranjan Sen Gupta, George Taylor, Margaret E. Thwaytes, T. E. M. Wardill, Norman Williams.

D.P.M.—J. C. Baillie, R. F. B. Bennett, F. H. Bodman, E. A. Burkitt, F. R. M. Calder, Sydney Catterall, G. I. Davies, R. H. Gaman, J. K. Hewat, R. M. Jones, F. J. Kelleher, Harold Lantin, Ivan Leveson, Amedeo Limentani, S. C. MacMillan, J. W. Macpherson, D. H. D. Paine, R. A. Sandison, R. B. Taylor, W. N. Taylor, D. C. Watt, Alexander Wood, C. M. Xavier, F. L. D. Young.

D.M.R.D.—D. M. R. Barry.

D.A.—R. V. Sturton.

Faculty of Anæsthetists.—The following were elected to the fellowship:

Dr. George Feneley, Dr. A. Parry Brown, Dr. H. Grant-Whyte, Dr. Geoffrey Kaye.

Faculty of Dental Surgery.—A course of lectures on anatomy, applied physiology, and pathology in their application to dental surgery, and on dental histology will begin on Jan. 24 and will continue until Feb. 18. Further particulars may be had from the secretary of the faculty.

Association of Surgeons of Great Britain and Ireland

The annual meeting of the association will be held in Dublin on May 26, 27, and 28 under the presidency of Prof. H. S. Meade. The programme includes discussions on Surgical Ritual (opening speakers, Sir Hugh Cairns, Sir Reginald Watson-Jones, Mr. Julian Taylor, Mr. F. Gill, and Mr. D. M. Douglas), Use and Abuse of Streptomycin, and End Results and Treatment of Injuries to Peripheral Nerves (Mr. H. J. Seddon).

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty on Jan. 10, with Dr. W. R. Snodgrass, the president, in the chair, the following were admitted to the fellowship: Max Benjamin Schwartz, Transvaal (qua physician); and William Woolf Frank, Queenstown (qua surgeon).

Faculty of Anæsthetists

The first annual meeting of the faculty will be held on March 16, at 3.30 P.M. At 5 P.M. the first Joseph Clover lecture will be given by Mr. A. D. Marston. On the same day the first anniversary dinner will be held; all fellows and members of the faculty are eligible to attend.

Scottish Surgical Pædiatric Club

The first meeting of this society was held in Glasgow on Dec. 17 and 18 and was attended by 27 members, who came from Aberdeen, Dundee, Edinburgh, Glasgow, and Inverness. A dinner was held in the Royal Faculty of Physicians and Surgeons on the 17th, and the next day four papers were read at the Royal Hospital for Sick Children in the morning, and clinical and pathological demonstrations were held in the afternoon. The next meeting will take place in Aberdeen in May.

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Harveian Society of London

The Buckston Browne prize for 1948 has been awarded to Dr. V. C. Medvei, for his essay on the Mental and Physical Effects of Pain.

Royal Institute of Public Health and Hygiene

On Thursday, Feb. 10, at 7.30 P.M., in the College of Art and Technology, at the Newarke, Leicester, Dr. J. Browning Alexander will deliver a lecture on the Catarrhal Child.

North of England Otolaryngological Society

A clinical meeting of this society will be held at the Eye and Ear Infirmary, Myrtle Street, Liverpool, on Saturday, Jan. 29, at 2 P.M.

London County Medical Society

At a meeting of the society held on Jan. 5, the following officers were elected: president, Dr. C. D. Coyle; vice-president, Mr. Iain Matheson; treasurer, Dr. L. T. Hilliard; secretary, Mr. J. Gabe.

Institutions Renamed

The Board of Control have decided that the Rampton State Institution, Retford, Notts, shall be renamed Rampton Hospital for Mental Defectives; and Moss Side State Institution, Maghull, near Liverpool, is to be renamed Moss Side Hospital for Mental Defectives.

Life Assurance Medicine

The third International Congress of Life Assurance Medicine will be held in Rome from June 6 to 9. The following subjects have been chosen for discussion: Medical Examination on Life Assurance (Openers, Prof. H. Courcoux, Paris, Dr. R. de Beden, Trieste); Influence of Heredity on Mortality (Prof. R. Sand, Brussels, Prof. V. Bisceglie, Catania); Heart Diseases and Life Assurance (Dr. H. D. E. Milders, Rotterdam, Dr. Terence East, London, Dr. J. R. B. Hutchinson, Washington, Dr. V. Mortensen, Copenhagen); Lessons of the War in Relation to Preventive Medicine (Prof. C. Richet, Paris, Dr. F. Kaufman, Zürich, Prof. G. Mazzetti, Florence, Dr. A. Starna, Rome). Further information may be had from the secretary of the Life Assurance Medical Society, Dr. Kenneth Dickson, 3, Lombard Street, London, E.C.3.

Dispensing in Hospitals

In many hospitals prescriptions for members of the staffs, if issued by one of the medical staff, are dispensed by the hospital pharmacist. The Ministry of Health announces that there is no objection to this practice. In some instances, however, hospital pharmacists have joined the pharmaceutical list of the local executive council in order to dispense N.H.S. prescriptions for the staff; the Ministry says that this is unnecessary and advises those who have joined for this reason to resign. N.H.S. prescriptions dispensed by hospitals should not be sent to the executive council or pricing officer of the area.

Hospitals in the National Health Service, if they have neither a dispensary of their own nor convenient arrangements with another hospital, are now at liberty to give to out-patients prescriptions to be dispensed by any chemist doing N.H.S. work. Special prescription forms, which are now being prepared, must be used.

Lister Institute

Dr. W. d'Auvergne Maycock has been appointed superintendent of laboratories at the Elstree branch of the institute. He will continue to act as adviser on blood-transfusion to the Ministry of Health and the War Office.

Dr. Maycock, who is 38 years of age, went to McGill University from this country with a Lord Milner memorial exhibition and graduated there in medicine in 1935, taking his English Conjoint qualification in the same year. He was awarded the Holmes gold medal and held the Francis J. Williams fellowship in medicine and clinical medicine and a demonstratorship in the pathology department at McGill before returning to England to work with a Leverhulme research scholarship at the Royal College of Surgeons. The subject of his investigations was shock, and on the outbreak of war he was sent to France as second-in-command of the Army Blood Transfusion Service unit at Dieppe. After the B.E.F. returned to England he was appointed second-in-command of the Army Blood Supply Depot at Bristol, and at the end of the war he was placed in charge of the depot, with the rank of colonel. He was a member of the team at Bristol which investigated the diagnosis and treatment of secondary shock, and he is also part-author of the British report on dextran appearing on another page of this issue. His other published work includes papers on intestinal strangulation and on vascular reactions of sympathectomised cats. For several years he has spent part of his time in experimental work at the Lister Institute.

South East Metropolitan Regional Tuberculosis Society

The general meeting of this society will be held at Preston Hall, Aylesford, Kent, on Saturday, Jan. 22, at 10.30 A.M.

King Edward's Hospital Fund for London

The Fund has received a further instalment of £150,000 from the Nuffield Trust for the Special Areas. In founding this trust Lord Nuffield provided that any sums that might be available by way of repayment of loans or otherwise should pass to King Edward's Hospital Fund. A total sum of £1,150,000 has now been received.

The Pharmaceutical Society has appointed their deputy secretary, Mr. F. W. Adams, to be secretary with Mr. H. N. Linstead, M.P., to enable the latter to carry on with his public work. Mr. Adams will also be registrar in succession to Mr. Linstead.

Births, Marriages, and Deaths

BIRTHS

ANDERSON.—On Jan. 12, in London, the wife of Dr. I. M. Anderson—a son.

DICKINSON.—On Jan. 12, in London, the wife of Mr. J. R. Dickinson, F.R.C.S.—a daughter.

KYNASTON.—On Jan. 11, at Ipswich, the wife of Dr. Roger Kynaston—a daughter.

MEARES.—On Jan. 8, in London, the wife of Dr. D. E. Meares—a daughter.

MORE NISBETT.—On Jan. 8, at Woking, the wife of Surgeon Commander J. G. More Nisbett, R.N.—a daughter.

PARSONS-SMITH.—On Jan. 13, in London, the wife of Dr. Gerald Parsons-Smith, O.B.E.—a son.

PRICHARD.—On Jan. 17, in London, the wife of Dr. J. S. Prichard, M.C.—a son.

WILLIAMSON.—On Jan. 4, at Newcastle, the wife of Dr. Martin Williamson, M.C.—a son.

DEATHS

CHAPMAN.—On Jan. 14, Edward Seymour Chapman, M.D. Glasg., F.R.C.S.E.

HUTCHINSON.—On Jan. 11, at Bournemouth, Leslie Thomason Rose Hutchinson, M.A., M.D. Camb., D.P.H., D.T.M. & H., lieut.-colonel, I.M.S. retd.

PATON.—On Jan. 11, John Hunter Park Paton, M.D. Edin.

SWAN.—On Jan. 15, at Eastbourne, William Travers Swan, C.B., major-general, A.M.S. retd, aged 87.

Diary of the Week

JAN. 23 TO 29

Monday, 24th

UNIVERSITY COLLEGE, Gower Street, W.C.1
4.45 P.M. (Physiology theatre.) Mr. P. Johnson, PH.D.: The Ultracentrifuge and Electrophoresis Apparatus in Protein Research. (First of four lectures.)

Tuesday, 25th

UNIVERSITY OF LONDON
5.30 P.M. (17, Bloomsbury Square, W.C.1.) Prof. F. A. Paneth, F.R.S.: Use of Radioactive Tracers in Biological Research. (First of two lectures.)

UNIVERSITY COLLEGE
5.15 P.M. Dr. E. Ashworth Underwood: Respiration. (Second of four lectures.)

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: Histopathology of the Skin.

EUGENICS SOCIETY
5.30 P.M. (Burlington House, Piccadilly, W.1.) Prof. L. S. Penrose: Work of the Galton Laboratory.

Wednesday, 26th

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, S.E.5
2.45 P.M. Prof. W. E. Le Gros Clark, F.R.S.: The Thalamus.

BRITISH ASSOCIATION OF PHYSICAL MEDICINE
5.30 P.M. (St. Thomas's Hospital, S.E.1:) Dr. J. H. Cyriax: How to Examine a Joint.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St. Vincent Street, Glasgow, C.2
5 P.M. Prof. J. R. Learmonth: Surgery of the Spleen.

Thursday, 27th

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, S.W.1
4.30 P.M. Neurology demonstration.

MEDICO-LEGAL SOCIETY
8.15 P.M. (26, Portland Place, W.1.) Dr. Robert Forbes: The Coroner, the Doctor, and the Public.

Friday, 28th

UNIVERSITY COLLEGE
5.15 P.M. Mr. F. Bergel, PH.D.: Pharmacological Chemistry. (First of three lectures.)

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES
8 P.M. (11, Chandos Street, W.1.) Dr. I. N. Orpwood Price: Modern Interpretations of Serum Tests.

MAIDA VALE HOSPITAL MEDICAL SCHOOL, W.9.
5 P.M. Dr. P. H. Tooley: Psychiatric demonstration.

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OBJECTS OF RESEARCH *

REORIENTATION TOWARDS COMMONER DISEASES

STANLEY ALSTEAD
M.D. Lpool, F.R.C.P. Lond., F.R.F.P.S. Glasg.
REGIUS PROFESSOR OF MATERIA MEDICA AND THERAPEUTICS IN THE UNIVERSITY OF GLASGOW

MEDICINE has its roots in the fundamental sciences, and it looks increasingly to physics, chemistry, and biology. Usually these sciences are stepping-stones to the profession of medicine. But to a small minority of doctors—those specialising, for example, in biophysics, biochemistry, or parasitology—medicine assumes a subsidiary position; it provides merely a background which lends colour to work which is often of much greater precision and complexity, and whose bearing on the medical problems may be difficult to define.

These circumstances have far-reaching effects on the pattern of research in medicine, and not all of them are beneficial. The growth of subdepartments remote from the hospital ward has favoured research which may contribute little or nothing to the immediate requirements of the sick man. Nevertheless, it is by laboratory workers that the great bulk of medical research is now done. This, I believe, is because teams of researchers can be most easily organised in the laboratory, where the worker can exercise control over his experiments and where he is insulated from the distractions which complicate even the simplest research schemes undertaken by clinicians.

Clinical research requires the consent and coöperation of the patient, which are unlikely to be forthcoming if the work involves him in financial loss, inconvenience, or other hardships. Furthermore, it is always open to the patient to abandon an experiment at any stage; and this not infrequently happens, though the clinician may have devoted much time and care to his investigations.

Research on man is important to the clinician because it creates and maintains a feeling of reality which can rarely be achieved in a laboratory remote from the wards. At the same time he cannot afford to ignore the many advantages of collaboration with his colleagues in the laboratory, and the realisation that clinical medicine is inseparable from the basic sciences may indeed be something of a menace to him. Evolved, as he is, out of the physiologist, the clinical investigator is continually looking back over his shoulder at the rabbits and cats, balloons and kymographs, and other impedimenta of the physiological laboratory. He must be constantly on his guard lest he finds himself side-tracked—enthralled, as it were, by the song of the sirens floating so sweetly from the department of physiology. Not for him the luxury of the definitive experiment. Let him ignore this warning and he will soon lose sight of his objective, represented by the sick man's disability; and the next step will be an attempt at psychological compensation characterised by an outpouring of publications which are the mere by-products of a major piece of research gone astray.

I submit that this trend is all too apparent in the medical research centres of the world today. Clinicians are becoming increasingly entangled in techniques, and to a serious extent in developing side-lines. Considering the volume of medical literature we may well recall a dialogue between Samuel Johnson and his biographer:

Johnson: Write a large book. Write a folio.
Boswell: But, Sir, will it be of any use?
Johnson: Never mind the use, Sir: write it.

* From an inaugural lecture delivered on Oct. 7, 1948.

RESEARCH ON WHAT?

One of the curious things about medical research is the large number of discoveries which have resulted from accidents. The happiest part of these accidents was the presence of a man with unusual powers of observation and the wit to appreciate the full significance of what he saw. The combination of these attributes is rare, and it is certainly not to be found in all whose concept of research is simply the elaboration of new advances. The discovery of the liver treatment of pernicious anæmia was not the outcome of logical deduction from physiological premises; and to this extent the discovery comes into the class of happy accidents. Now the effect of this momentous discovery was the releasing of a vast number of workers on the whole subject of blood diseases and the physiology of blood formation. I do not maintain that this great effort has been in vain; but it is remarkable that when research takes on this form it dissipates itself over an enormous field, and any further advance comparable with the original discovery is rare. The researcher's attempts to predict new therapeutic advances from previous discoveries have nearly always proved disappointing.

There is a further reason for choosing pernicious anæmia as an illustration. It is a comparatively rare disease; and I feel most strongly that as research-workers we are excessively concerned with the minutiæ of uncommon diseases while the common and disabling maladies receive far too little attention.

In general the interest of doctors and students in their patients is proportional to the acuteness and gravity of the disease. Two types of case are most eagerly sought after: first the "collector's piece," and secondly that of acute illness in a young patient, where the tendency to spontaneous recovery is greatest. What bearing has this on trends in medical research? My answer is that these characteristics are often closely linked with social factors and hospital policy, and these in turn determine the disposal of the case.

THE OLD AND UNINTERESTING

Notwithstanding the graduation of the old poor-law hospital to municipal and then to national status, practitioners in the main continued to send their young and acutely ill patients to the voluntary hospitals. The obvious reason for this differentiation was that whereas the municipal hospitals have always been under a statutory obligation to admit any patient properly referred to them, the voluntary hospitals have retained the power to determine what type of patient should be admitted. Attempts to justify this practice have included reference to tradition, expediency, staffing arrangements, accommodation, and equipment.

But very few members of the staffs of former voluntary hospitals have any conception of the adverse effect which the care of the senile and incurable has had on the medical and nursing staffs of other institutions. To attain to a kindly and gracious old age is not the happy lot of everybody; and avoidance of the humiliations of senility demands considerable intellectual power and unfailing self-discipline, the foundation of which must be laid in childhood. Only direct experience can bring realisation of the depressing effect of the senile patient who is also apathetic, uncouth, and even offensive. By contrast, the nurse caring for the acutely ill young subject can be almost certain that skilful attention for a comparatively short time will be rewarded by his recovery; and with the establishing of convalescence she has the solid satisfaction of knowing that she has made an important contribution. Furthermore, the young and alert are usually less forgetful of their obligation to acknowledge their gratitude to the nursing staff. As to the physician, can it be doubted that he will grow stale and lose heart

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if overwhelmed by a preponderance of long-term senile patients with incurable diseases?

My plea is for reorientation of our attitude. The complexity of the problem and its social ramifications make it practically certain that a solution, if found at all, will come only from multilateral approach; inevitably the close coöperation of the social scientist and the almoner will be required. I submit, too, that the coincidence of old age with illness or disability is too often regarded as justifying neglect of valuable therapeutic possibilities. The widespread tendency to discourage admission of the aged sick has robbed the profession as a whole of exceptional opportunities for clinical research. A growing realisation during the past decade of the need to investigate and treat the diseases of old people, has led to the creation of yet another specialty—geriatrics. I doubt the wisdom of this development; for I cannot accept the implication that the ordinary care of the aged calls for the services of a specialist. Their care is as much the responsibility of the general practitioner and general consultant as is the care of any other type of patient. How much more important it is that the medical student should receive systematic instruction from the experienced general physicians of the teaching unit than that the seal of specialism should be laid on these cases by the geriatrician.

GERIATRICS IN THE GENERAL WARD

It is agreed that medical teaching and research should not be completely dissociated; and this is particularly true of geriatrics. Teaching on a difficult case is a recognised method of defining the research-worker's problems. For the same reasons it is highly desirable that the aged and chronic sick should ordinarily be accommodated in the general medical wards and not segregated in some special and possibly remote wing of the hospital. Authoritative writers have recommended such concentration of the aged sick, but although this may have some administrative advantages I do not see how it can be other than bad for the patient, the nurse, and the doctor. It is far better to distribute these patients among all the wards and thus spread the burden.

In his own ward let the visiting physician be confronted by his aged patient, whose disability is often difficult to define in ordinary medical terms, and whose treatment and general management may tax all the resources of the hospital. And if the physician is defeated, let him admit it. This in itself will provide a significant experience in the medical student's education. Time devoted to this subject will certainly not be wasted, for the student once qualified will deal with similar cases every day in general practice.

As far as our centres of teaching and research are concerned, the history of therapeutics in relation to the chronic and aged sick has been almost entirely one of retreat, mainly by diverting or transferring such patients to other hospitals. But this practice is coming to an end. With regionalisation of admissions, every hospital will presumably have the opportunity of conducting teaching and research on patients of this type. Such research will largely consist in an attack on established disabilities, with an eye to preserving or restoring function rather than to æsthetic or other abstract considerations; superlatively important is the investigation of means of keeping patients on their feet. In the course of such research the physician may find himself changing imperceptibly into a surgeon, but he should not be unduly alarmed about this. One of the compensations may be that surgeons interested in the physician's problems may also undergo a becoming metamorphosis.

On the social side there are great opportunities for research, by non-medical as well as medical workers, into the best methods for relieving the loneliness of patients, stimulating their interest, maintaining a follow-up, and in many other ways arousing the patient to the various social interests and activities.

In the past a great deal of first-class research has been done by men who were certainly not geniuses but who found their problems in clinical work and focused their attention on a disease. They maintained their interest by living among the sufferers, and they persevered on simple lines until their work was successfully concluded. Theirs is an example better worth following than that of the increasing number of physicians who, after a promising start, are found becalmed in the doldrums of techniques and mechanisms.

BLOOD CHANGES IN PERITONITIS

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THE cause of death in peritonitis and the mechanism of the circulatory collapse which precedes death are in many cases obscure. We record here an investigation of certain factors which may affect the circulation directly or indirectly during the course of peritonitis; in particular the plasma and blood volumes and the levels of total circulating plasma-protein, plasma-albumin, and hæmoglobin were estimated in patients under the conditions of routine treatment.

We studied 35 patients with severe peritonitis; nearly all were sufficiently ill at some time to give cause for anxiety, and 12 eventually died. Operation was done in 33 cases, and other measures included intravenous infusion of physiological saline solution and 5% dextrose solution combined with suction drainage of the stomach to prevent or treat ileus. Systemic penicillin therapy was used for pulmonary infections, and in some cases sulphonamides were given as well.

As soon as practicable after the patient had been admitted to hospital and at intervals thereafter the plasma and blood volumes, and the plasma levels of proteins, albumin, sodium chloride, and urea were estimated. Fluid intake and output, urinary chlorides, and the usual clinical observations, including blood-pressure readings, were charted throughout. Bacteriological cultures and films were made from the peritoneal exudate obtained at operation. Other tests were added in some cases.

Plasma volume was measured by the Evans-blue ('T-1824') method. Dye concentrations were estimated with a photo-electric absorptiometer, checked in many cases with a spectrophotometer. In most estimations three blood samples were taken at 10, 20, and 30 min. after the dye had been injected. On occasion, however, it was impracticable to obtain multiple blood samples; so all calculations of plasma volume have been made from the dye concentration of the plasma at 10 min. after injection. The validity of this method of using a single 10-min. sample has been discussed by Davis (1942) and Gregersen (1944). To avoid stasis while withdrawing blood we punctured the femoral vein or artery in very ill patients, and to prevent hæmolysis we used a small quantity of liquid heparin as an anticoagulant. The figures of plasma and blood volumes given here are uncorrected for the small error due to dilution by heparin (about 2% for blood volume).

Blood volume was calculated in the usual way from the plasma volume and hæmatocrit reading (Wintrobe). No correction was made in the hæmatocrit figures for plasma trapped in the cell column. Hæmoglobin was estimated by the alkaline-hæmatin method (Clegg and King 1942) with the photo-electric absorptiometer, checked by oxygen-capacity measurements and by the artificial standard of Gibson and Harrison (1945). Protein estimations were done by the micro-

* In receipt of a personal grant from the Medical Research Council.

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Kjeldahl method. From these data the total circulating plasma-protein and albumin and total circulating hæmoglobin were calculated.

NORMAL VALUES

The normal values of plasma and blood volumes in most of the patients who recovered were obtained by estimations made after convalescence. For others —e.g., in fatal cases—we were obliged to calculate the probable normal values from height and weight measurements, and for this purpose we used figures from a series of 30 "healthy" patients in a surgical ward who had recovered from minor surgical ailments; the two groups of patients were roughly similar as regards nutritional state, height, weight, sex, and age. Identical methods of estimation were used in both series (the estimations in the healthy series were made by Drs. C. D. L. Cromar, S. Konstam, and W. C. Wilson). The average normal figures for plasma and blood volumes, based on body-weight, resembled closely those given by Gibson and Evans (1937), Harington et al. (1940), and Gregersen (1944); of 18 males the average plasma volume was 47·2 ml. per kg. (S.D. ± 5·3) and the average blood volume 84·9 ml. per kg. (S.D. ± 9·6). Like others, we found a wide range of normal values, even when correlated with body-weight or surface area—for instance, the plasma volume of males ranged from 39 ml. per kg. to 60 ml. per kg. Clearly it is important not to attribute a spurious accuracy to calculation of probable normal values and deficits.

To determine the effects of operation and confinement to bed for 1 or 2 weeks, we estimated plasma and blood volumes in patients without peritonitis before and after simple abdominal operations, such as appendicectomy. Little or no change was found. In this and the "healthy" series a surprisingly close correspondence was found between repeated estimations (usually within 6% for plasma volume). In cases of peritonitis, however, changes of less than 15% have been regarded as not significant.

Our volume figures in all series were probably somewhat higher than the true plasma and blood volumes. It is now generally agreed that the dye-hæmatocrit method gives blood-volume figures significantly higher than those obtained by other methods, and three points of our technique tend to raise the plasma-volume figures: dilution by liquid heparin; the use of plasma instead of serum; and calculation from 10-min. samples instead of from extrapolation of the disappearance curve. Our average normal figures, however, were only very slightly higher than those given by other workers. Moreover, we were concerned not with absolute values of plasma and blood volumes but with changes taking place in peritonitis, and the figures in all series were comparable.

In calculating normal total circulating protein, albumin, and hæmoglobin we assumed the following values as normal: plasma-protein 6·5 g. per 100 ml.; albumin-globulin ratio 1·7 : 1; and hæmoglobin 15·8 g. per 100 ml.

BLOOD-VOLUME CHANGES AND CLINICAL FEATURES

A general pattern of behaviour could be traced in the plasma and blood volumes, but considerable variation was found. The behaviour was more regular in cases of recovery than in fatal cases, and it is convenient to describe them separately.

In Cases of Recovery

A significant reduction of blood volume was found at the first estimation, usually before operation, in 11 of 23 recovery cases (fig. 1). There was no reduction of blood volume and no important circulatory disturbance in early peritonitis—e.g., during the first few hours after perforation of a peptic ulcer—no matter how intense and diffuse the peritoneal irritation. Reduction was found only in more advanced cases—e.g., 8 or more hours after perforation of an ulcer—and in cases of peritonitis from causes other than perforated ulcer when the peritoneal exudate contained many bacteria. The plasma volume was mainly involved, but the cell volume was also lowered; and the fall at this stage was between 20% and 30% of normal values. There were, however, none of the usual clinical signs of acute oligæmia (oligæmic shock); circulatory efficiency, judging from blood-pressure, pulse volume, skin colour, and temperature, was not obviously impaired. The only indications of a serious illness were an increased pulse-rate and a dusky tint in the facial flush.

The reduction of blood volume was associated with ileus or a large peritoneal exudate or both. Ileus was diagnosed when the small intestine was found to be distended at operation; copious and frequent vomiting before admission to hospital was not common. Ileus was often precipitated or aggravated by operation, after which quantities of dark green or brown material containing altered blood were removed by gastric suction. The chief symptoms were: distress, mainly from abdominal distension and pain; inability to rest or sleep well; and weakness; to which the usual features of dehydration were added if fluid loss exceeded replacement. The blood-pressure remained normal. When intravenous infusion was given in adequate amount, the blood volume rose to normal or above normal, the rise being almost entirely in the plasma volume. In a few cases

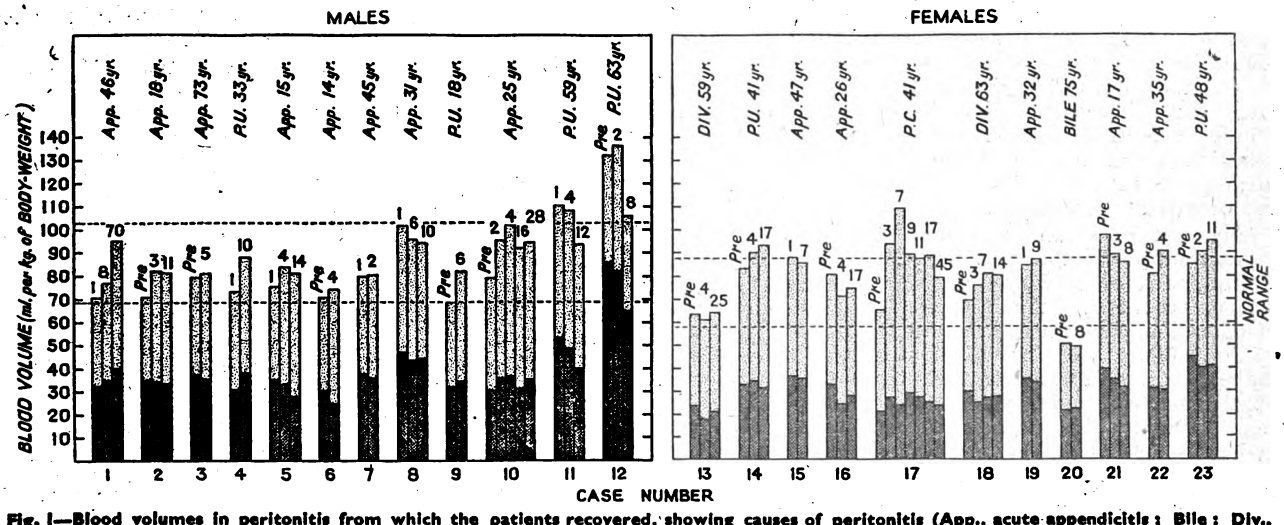

Fig. 1—Blood volumes in peritonitis from which the patients recovered, showing causes of peritonitis (App., acute appendicitis; Bile; Div., diverticulitis; P.C., perforated colon; P.U., perforated peptic ulcer); age of patient; time of estimation (Pre, preoperative or days after operation); plasma volume (stippled columns); and cell volume (hatched columns).

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a small rise was found also in the cell volume during the first 2 days, which suggested that a proportion of the cells had previously been trapped in some part of the vascular bed. After operation oliguria was almost invariable, even when the blood volume rose and a positive fluid balance was obtained; the urinary output remained less than a litre for 2–5 days. In some cases the cell volume fell from about the 4th day and was still reduced 2 weeks after operation. This fall was compensated in some cases by a rise in plasma volume, but in others the plasma volume remained stationary and the blood volume declined (cases 11, 12, 16, 21).

Three unusual cases require mention: case 12 was one of polycythæmia vera and an abnormally high blood volume; case 20 was one of unusually low volume; and case 17 showed a remarkable increase of plasma volume on the 7th day, when chloride retention and oliguria were present during large intravenous infusions of saline solution, the increase in cell volume on the 3rd and 9th days being the result of blood-transfusions.

In Fatal Cases

The volume changes are shown in fig. 2. The variation in behaviour was great, as would be expected from the

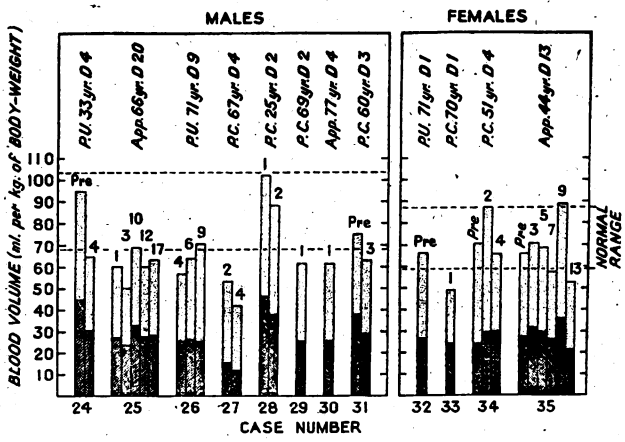

Fig. 2—Blood volumes in fatal peritonitis, showing details as in fig. 1, except that in cases 26, 28, and 33 the numerals on top of the columns show the days after onset of peritonitis, and the day of death—e.g., D4—is also indicated.

widely differing clinical and pathological circumstances. Examples of variation were: a large fall of blood volume from an initial normal level (case 24); a persistently reduced level (case 25); a steady rise from a low level (case 26); and a terminal steep fall from a high normal level (case 34). These cases are described in greater detail below. Generally, reduction of blood volume at the first estimation was more common and rather larger than in cases of recovery, probably because the illness in fatal cases was more severe and of longer duration; and the blood volume did not rise with intravenous infusion, or a further but not always large fall occurred before death.

The most consistently fatal form of peritonitis followed perforation of the colon. When the soiling of the peritoneum was of moderate degree, and further soiling was prevented by exteriorisation of the affected bowel at operation, the patient survived for 3 or 4 days (cases 27 and 31). After operation the condition steadily deteriorated, with or without evidence of ileus, but with apathy and weakness, cyanosis, a sluggish skin circulation, a rapid pulse, oliguria, a rising blood-urea level, and a low concentration of urinary chloride with a normal or slowly falling plasma-chloride level. The blood-pressure remained normal and the pulse of fair volume till the final collapse of the circulation began 6–12 hours before death. Then the blood-pressure fell quickly, the pulse became weak and finally impalpable, the hands cool, the skin clammy with sweat and of a mottled livid colour, the facial skin venules prominent, the eyes sunken and dark-ringed, and apathy was succeeded by stupor and prostration. The blood volume at this terminal stage had fallen from the preoperative level (case 31), but the fall was not very great and was probably insufficient to explain the circulatory collapse. The course was not obviously influenced by large volumes of intravenous fluid.

After gross flooding of the peritoneum with fæces from a larger perforation of the colon (cases 33 and 34) the features of the terminal phase appeared almost at once, certainly within 1 or 2 hours. In case 33 the blood volume was very low 8 hours after perforation and 3 hours before death, but in case 34, though a steep fall had taken place with the loss of 1 litre of plasma in about 7 hours, the blood volume was still within the presumed normal limits when the circulation had collapsed completely. Death took place too quickly for ileus to have much, if any, effect.

Cases 28 and 35 require special mention. In case 28 there was a sudden gross leakage from the colon, the result of a technical error made at a previous operation. The blood volume was high on the 1st day of peritonitis; it fell on the 2nd day (the fall was mainly in the cell volume) but was still at a satisfactory level. The patient died during a second operation a few hours after this estimation. In case 35 intravenous infusion was omitted until the 6th day, when an initially mild ileus had become definite. A very severe pyrogenic reaction at the start of intravenous infusion complicated the course, which was distinctly unusual.

CIRCULATING PLASMA-PROTEIN

The changes in total circulating plasma-protein followed very closely the changes in plasma volume. When the plasma volume fell, the total circulating protein showed a fall of similar magnitude, but in most cases the fall in circulating albumin was proportionately greater. When the plasma volume rose with intravenous infusion, the total circulating protein rose, but not the circulating albumin; the albumin deficit persisted for about 2 weeks or even longer. Evidently protein in the form of globulin was very mobile and passed equally readily into and out of the circulating plasma. Albumin was much less easily mobilised, and its regeneration was slow. Generally, the plasma-protein concentration remained remarkably constant in the presence of considerable volume changes and despite large infusions of non-protein fluid.

The changes in the level of circulating protein and their relation to volume changes are illustrated in tables I and II (deficits of 15% or less are not shown). Short clinical details of the cases cited in the tables are given below.

CASES OF RECOVERY (TABLE I)

Case 2.—A boy, aged 18, was admitted 6 days after the onset of symptoms of acute appendicitis. He had not vomited. A very large pelvic abscess was present and was drained through the rectum. There was no ileus.

A 30% reduction of plasma volume was found on admission. All deficits, except that of circulating albumin, were rapidly restored by intravenous infusion given for 4 days after operation.

Case 5.—A boy, aged 15, was admitted 7 days after the onset of symptoms of acute appendicitis. Peritonitis had probably been present for 4 days. At operation a perforated appendix and diffuse peritonitis with copious purulent exudate were found. After appendicectomy and drainage, intravenous infusion for 3 days and penicillin 11,000,000 units in 7 days were given. Recovery was complicated by pulmonary collapse and pneumonia for 10 days and mild ileus for the first 3 postoperative days.

The volume and protein changes were similar to those in case 2 but with the addition of a moderate fall of cell volume.

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TABLE I—CHANGES IN PLASMA AND BLOOD VOLUMES AND IN TOTAL CIRCULATING PROTEINS IN CASES OF RECOVERY

Case no.	Estimation No.	Estimation Time	Plasma Volume (ml.)	Plasma Volume (ml./kg.)	Plasma C.D.	Blood Volume (ml.)	Blood Volume (ml./kg.)	Blood C.D.	Total circulating proteins: Plasma-protein (g.)	C.D.	Plasma-albumin (g.)	C.D.	Clinical condition
2	1	Preop.	2128	35·47	29%	4173	69·55	16%	157	20%	?	?	Fair
	2	3 days postop.	2937	48·95	..	4978	82·97	..	182	..	86	30%	Good
	3	11 days postop.	3000	50·00	..	4959	82·65	..	198	..	88	28%	Good
5	1	13 hr. postop.	2152	39·85	23%	4060	75·19	..	172	..	76	34%	Fair
	2	4 days postop.	2765	51·17	..	4533	83·94	..	216	..	97	16%	Fair
	3	14 days postop.	2845	52·80	..	4377	81·06	..	219	..	79	31%	Good
16	1	Preop.	2444	47·00	..	4142	79·65	..	165	..	84	16%	Fair
	2	4 days postop.	2462	47·35	..	3675	70·67	..	159	..	62	38%	Fair
		17 days postop.	2403	46·21	..	3845	73·88	..	159	..	82	18%	Good

C.D. = Calculated deficit. Deficits of 15% or less are not shown.

Case 16.—A woman, aged 26, was admitted 3 days after the onset of symptoms of acute appendicitis. At operation diffuse peritonitis with copious purulent exudate and a perforated appendix were found. After appendicectomy and drainage, intravenous infusion was given for 3 days. A residual pelvic abscess was drained through the rectum on the 12th day. There was no ileus.

The main features were steady levels of plasma volume and of total circulating protein, and a fall in cell volume and in circulating albumin on the 4th day, with some recovery by the 17th day.

FATAL CASES (TABLE II)

Case 24.—A man, aged 33, was admitted 8 hours after perforation of a duodenal ulcer. At operation a copious turbid exudate was found, from which intestinal organisms were grown on culture. The perforation was closed without drainage. Intravenous infusion and gastric suction was given from operation to death. Very severe ileus and oliguria developed, and large amounts of fluid were lost from the stomach, exceeding replacement. The circulation collapsed 9 hours before death on the 4th day. A necropsy showed gross purulent peritonitis and pneumonia.

The values at the first estimation were normal, except that the level of total circulating protein was unusually high. Shortly before death all values, including cell volume, showed large falls, the greatest being in the level of circulating albumin. Oligæmia and renal failure were probably an important cause of death.

Case 25.—A man, aged 66, was admitted 4 days after the onset of acute appendicitis; peritonitis had probably been present for 2 days. At operation diffuse peritonitis with copious purulent exudate and a perforated appendix were found. After appendicectomy and drainage, severe ileus was present for the first 5 days, incontinence of fæces from the 6th day to death, frequent watery stools from the 6th to the 10th day, oliguria and azotæmia from the 5th day to death, and hypotension and stupor from the 16th day to death. Intravenous infusion was given for the first 10 days, and gastric suction for the first 6 days. Sulphonamides and penicillin 4,000,000 units were also given. The patient died on the 20th day. A necropsy showed multiple intraperitoneal abscesses and pneumonia.

All values at the first estimation were low and fell further during ileus; recovery occurred later to initial but not to normal levels. The greatest deficit was in circulating albumin. The volume changes did not reflect the clinical state, which deteriorated steadily. Renal failure was a definite feature of the late stages.

Case 26.—A man, aged 71, had a perforated stomal (gastro-jejunal) ulcer with signs of slowly spreading peritonitis for 4 days before estimations were begun. There was no operation. Gastric suction, intravenous infusions, and penicillin 4,000,000 units were given from the 4th day to death. There was severe ileus from the 4th to the 7th day, but fluid replacement exceeded losses. The urinary output was satisfactory from the 4th to the 9th day. The blood-urea level was high but steady throughout. The patient died on the 9th day. A necropsy showed diffuse purulent peritonitis and pneumonia.

All values were low at the first estimation on the 4th day. Subsequently the plasma volume and total circulating protein rose to normal or near normal values, while cell volume and circulating albumin remained at reduced levels; circulating albumin was disproportionately low. Deterioration was steady and the circulation finally collapsed, in spite of the rise in plasma and blood volumes. Oligæmia and renal failure almost certainly played no important part in the fatal result.

Case 34.—A woman, aged 51 years, was admitted 2 days after the onset of symptoms of peritonitis. At operation she was found to have diffuse peritonitis with copious purulent exudate and perforation of a carcinoma of the pelvic colon (apparently sealed off). After drainage and colostomy, the patient was treated with intravenous infusion and gastric suction for the first 3 days, and steadily improved till the 4th day, when a further large perforation occurred, flooding the peritoneal cavity with fæces. There was almost immediate circulatory collapse, and death took place 13 hours later.

TABLE II—CHANGES IN PLASMA AND BLOOD VOLUMES AND IN TOTAL CIRCULATING PROTEINS IN FATAL CASES

Case no.	Estimation No.	Estimation Time	Plasma Volume (ml.)	Plasma Volume (ml./kg.)	Plasma C.D.	Blood Volume (ml.)	Blood Volume (ml./kg.)	Blood C.D.	Total circulating proteins: Plasma-protein (g.)	C.D.	Plasma-albumin (g.)	C.D.	Clinical condition
24	1	Preop.	3442	50·62	..	6494	95·50	..	224	..	131	..	Fair
	2	4 days postop.	2356	34·65	32%	4445	65·37	32%	198	..	83	45%	Dying (4 hr. before death)
25	1	16 hr. postop.	2532	33·76	28%	4562	60·83	29%	159	31%	78	46%	Ill
	2	3 days postop.	2090	27·87	41%	3870	51·60	40%	122	47%	72	50%	Ill
	3	10 days postop.	2765	36·87	22%	5217	69·56	18%	166	29%	101	30%	Ill
	4	12 days postop.	2475	33·00	30%	4583	61·11	28%	176	24%	95	34%	Very ill
	5	17 days postop.	2605	34·73	26%	4736	63·15	26%	164	33%	99	32%	Very ill
26	1	4 days after onset	2000	31·25	34%	3636	56·81	33%	131	33%	71	42%	Fair
	2	6 days after onset	2391	37·36	21%	4053	63·33	26%	158	19%	68	45%	Ill
	3	9 days after onset	2853	44·58	..	4458	69·66	..	163	17%	66	46%	Dying (12 hr. before death)
34	1	Preop.	2247	46·81	..	3364	70·08	16%	146	..	92	..	Ill
	2	2 days postop.	2817	58·69	..	4204	87·58	..	172	..	98	..	Fair
	3	4 days postop.	1786	37·21	21%	3189	66·44	20%	105	28%	80	..	Dying (6 hr. before death)

C.D. = Calculated deficit. Deficits of 15% or less are not shown.

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There was no evidence of ileus. A necropsy showed gross fæcal contamination of the peritoneum.

On admission the plasma volume was normal in spite of pronounced hypochloræmia. On the 2nd day the plasma and cell volumes had increased significantly. On the 4th day, 7 hours after the second perforation, the plasma volume had fallen considerably below the preoperative level, with a parallel fall in total circulating protein, a stationary cell volume, and therefore considerable hæmoconcentration. Assuming that the values on the 2nd day were maintained until the second perforation, it was calculated that a litre of plasma had been lost in about 7 hours. Nevertheless, the blood volume was still within the normal limits when circulatory collapse was complete. The level of circulating albumin did not fall so quickly as the plasma volume and the total circulating protein.

OTHER CHANGES

Hæmoconcentration was not a notable feature of peritonitis. Except in a few cases of pre-existing anæmia the hæmoglobin and hæmatocrit levels were normal or slightly increased at the first estimation; the highest hæmatocrit reading in the series (apart from the case of polycythæmia) was 51%. Subsequently, in recovery cases the levels fell steeply when the plasma volume rose and the cell volume remained steady or declined; in fatal cases the fall was usually much smaller, and, in the case of very rapid plasma loss (case 34), hæmoconcentration occurred. A point of practical significance was that changes in hæmoglobin, hæmatocrit, and plasma-protein concentration provided no reliable indication of the volume changes.

Plasma and Urinary Chlorides.—Plasma-chloride concentration was below normal in many cases on admission, presumably as a consequence of ileus, and the urinary chlorides were low or absent. When ileus developed for the first time after operation, the plasma-chlorides remained normal for 1 or 2 days, or fell slowly, but urinary chlorides disappeared promptly. With intravenous infusion of saline solution both plasma and urinary chloride levels usually rose steadily, but the behaviour was distinctly erratic. Sometimes there was salt retention, and chlorides could remain absent from the urine after the plasma-chloride level had been completely restored and the patient had recovered fully from ileus. In other cases a fair concentration of urinary chlorides was noted when the plasma-chloride level was low and rising very slowly. These abnormal relations between plasma and urinary chlorides persisted for some days. In general there was no good correlation between plasma-chloride concentration and plasma volume on admission or subsequently.

Azotæmia was common, especially during severe ileus, and also when circulatory failure appeared. It was more frequent in elderly than in young patients. Analysis of our results, however, would be unprofitable without a more complete investigation of renal function than we have yet carried out.

Liver Injury.—The slow regeneration of plasma-albumin suggested injury to the liver, which has been confirmed by thymol-turbidity and bromsulphthalein-retention tests. This subject is under investigation and is not considered here.

Cardiac Output.—By the method of Cournand et al. (1943) a few estimations were made of cardiac output in the late stages of fatal peritonitis. Arteriovenous oxygen difference was greatly increased though the arterial-blood oxygen was reduced, probably by pneumonic consolidation. Right auricular pressure was normal or slightly below normal. Measurement of oxygen consumption in these prostrated uncoöperative patients was difficult, and the results were of doubtful reliability. The calculations, however, indicated a low cardiac output.

Stasis in the Skin Circulation.—Stasis in the minute vessels of the skin was sometimes evident during the last few days of fatal peritonitis, while the blood-pressure was still normal and the pulse of good volume. When the circulation finally collapsed, the appearance of the skin suggested almost complete stagnation, particularly in the extremities. The relation of stasis to blood-volume changes and the mixing of injected dye were investigated as follows:

Samples of skin blood were obtained by incising the finger-tip or the nail fold, and samples of venous blood from an elbow vein of the same arm, which had been previously warmed. The rate of bleeding from the incision indicated roughly the rate of blood-flow in the skin. Venous blood was withdrawn at 10 min. and 30 min. after injection of dye for blood-volume estimation, and finger blood was collected between 10 min. and 30 min. after the injection. The dye concentration in finger blood was compared with the average dye concentration of the venous samples.

Until the terminal collapse of the circulation began, the dye concentrations in finger and venous blood were practically identical, though the blood-flow in the skin had become very sluggish. But in the terminal stage of collapse the dye concentration was much lower in the skin blood than in venous blood. Probably the skin blood then was largely stagnant blood which the dye had not reached, with a small admixture of circulating blood containing dye. Since the plasma volume in these cases did not fall greatly after the onset of circulatory collapse, the proportion of the total blood volume which had become completely stagnant was probably small.

Bacteriology.—For the first 6 hours after perforation of a peptic ulcer the peritoneal exudate showed no growth on culture and no organisms in films. Between 6 and 12 hours after perforation no growth on culture was the rule and few organisms were present in films, but at later periods intestinal organisms were present in both. In cases of appendicitis and peritonitis from other causes the exudate contained the usual mixed intestinal flora, with a predominance of coliform organisms. In fatal cases *Cl. welchii* were looked for but were not found in the peritoneal exudate, and there was no evidence of *Cl. welchii* septicæmia.

DISCUSSION

It was unlikely that serious errors in estimating plasma volume arose from the abnormal conditions imposed by peritonitis. A suspected error was an erroneously high reading of plasma volume due to abnormal escape of dye, but there was no suggestion from the clinical condition that the true blood volume was much lower than the estimated value. The dye disappearance curves of many cases did not indicate abnormal escape of dye; the curve during the stage of acute inflammation was very similar to that after recovery. It is assumed that there was no important discrepancy between the true and estimated volumes.

Mechanism of Volume Reduction

In the present series, ileus with large fluid losses from the bowel was often associated with reduction of plasma volume and was no doubt an important cause of the reduction. But reduction was sometimes found in peritonitis when ileus was absent, and in the case of massive fæcal contamination of the peritoneum the plasma volume fell steeply before ileus could have had much effect. The likely cause then was loss of plasma by exudation into the peritoneal cavity and into the extensive area of inflammation. Presumably both mechanisms acted simultaneously in most cases. There was no evidence that reduction of plasma colloid osmotic pressure played any important part in the reduction of plasma volume; the total plasma-protein concentration remained remarkably constant, and in many cases of recovery the plasma volume was well maintained in the presence of low or falling levels of plasma-albumin and of total circulating albumin. Our investigations showed

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that the blood stagnated in the skin only during the terminal stage of the illness, and that stagnation was responsible for a rather small further reduction of the actively circulating volume.

Reduction of cell volume was more puzzling than reduction of plasma volume. The cell volume did not fall when plasma was lost by rapid peritoneal exudation, and therefore the fall was the result of a somewhat slow process. The fall was sometimes continuous over many days. We suggest that part of the explanation may be found in the vascular changes which occurred in the obstructed, distended, and inflamed bowel. During ileus the fluid removed by gastric suction, often in large amounts, contained altered blood which had been extravasated into the intestinal wall and lumen, and the volume of cells thus lost may have been considerable. This point is being investigated. Ileus, however, was apparently not the only mechanism involved, because the relation between the fall and ileus was inconstant.

But, if ileus and peritoneal exudation were probably the main causes of volume reduction, there was much that remained uncertain—e.g., why in certain fatal cases large infusions did not raise the low level of plasma volume or even prevent a further fall. Evidently some process more complex than simple fluid depletion was at work.

Effects of Volume Reduction

In recovery cases the usual initial reduction of blood volume (by 20–30% of normal values) produced none of the usual features of acute oligæmia, such as hypotension. Probably the fall in volume was slow and gradual enough to allow adaptive processes to develop, and the condition at this stage might be called one of subacute oligæmia. Ordinary methods of clinical examination revealed no serious circulatory abnormality, but it was almost certain that circulatory disturbances were present. During the first few days after operation oliguria persisted in spite of full rehydration, and abnormal relations existed between plasma and urinary chlorides; these could be attributed to the continued effects of previous renal injury. In some fatal cases with persistent or progressive oligæmia impairment of renal function was obviously severe, and renal failure was probably an important cause of death. During this prolonged oligæmia the blood-pressure was not below normal and the pulse remained of fair volume, yet the renal injury inflicted could be irremediable, though it was not invariably so. Sanderson (1948) found in 4 cases of "abdominal catastrophe" that the glomerular filtration-rate and effective renal plasma flow were reduced, sometimes very greatly, giving a general picture of renal ischæmia, which persisted for some time after dehydration had been corrected. How frequent these changes are, in peritonitis, has still to be determined, but there seemed a distinct possibility in our cases that renal vasoconstriction occurred when the blood volume was reduced.

Apart from considerations of renal failure, oligæmia was an immediate cause of death in some cases, since the blood volume was so greatly reduced that the circulation could not be maintained, and oligæmia must have been a major factor in the terminal circulatory collapse. But in others the blood volume shortly before death was one at which the circulation could have been carried on efficiently. There was good evidence from this series that the final failure of the circulation did not invariably depend on oligæmia. Emerson and Ebert (1945) made similar observations in cases of penetrating abdominal wounds and peritonitis; they reported 3 cases where the blood volume was normal shortly before death. And Cournand et al. (1943) mentioned a case of fatal abdominal injury and peritonitis with the blood volume nearly normal during profound "shock." In a few of our cases the blood-pressure and cardiac output were low during the last few hours of the illness, and stagnation of blood in the skin vessels was conspicuous; yet the right auricular pressure and blood volume in these cases were normal or only slightly reduced. Evidently the circulatory machinery had become completely disorganised. The cause of the disorganisation was not at all clear, but on many grounds, especially the association with heavy bacterial contamination of the peritoneum, it seemed not unreasonable to suspect bacterial intoxication.

The effects of bacterial infection on the circulation were very difficult to assess. By its local action in the peritoneum it was responsible for ileus and peritoneal exudation and thus indirectly for oligæmia. In cases of special severity it may in some way have prevented the correction of oligæmia. But, irrespective of oligæmia, a direct action on some parts of the circulatory apparatus whereby the efficiency of the circulation was destroyed seemed highly probable.

Practical Applications

This investigation provided a few hints on treatment, though it was not designed with that object. The most important indication was that oligæmia should be corrected as early as possible in the course of the illness to avoid or mitigate the serious and insidious risk of renal failure. For restoring and maintaining the blood volume intravenous non-protein fluid was usually effective, and significant dilution of plasma-proteins was not observed. Why it failed in some instances was not determined, and whether plasma or blood would have been better was not investigated. Blood, presumably, would be preferred to plasma because of the reduction of cell volume which was sometimes responsible for the continued fall in blood volume. Whether plasma or blood would have saved patients with heavy bacterial contamination of the peritoneum seemed extremely doubtful. Certainly experience of peritonitis from penetrating abdominal wounds during the late war provided little encouragement; many wounded men with established peritonitis showed a transient or poor response to resuscitation by blood-transfusion. Recently we have seen a patient with advanced peritonitis from perforation of a peptic ulcer which was mistaken for gastro-intestinal hæmorrhage; he was given a large transfusion of blood without obvious effect on the failing circulation or on the time of survival.

A final point was the frequency of pulmonary complications in fatal peritonitis. Collapse of the lung bases was very commonly found post mortem in the presence of even a moderate degree of abdominal distension. Pneumonic consolidation was surprisingly frequent and developed in spite of large doses of penicillin; possibly the penicillin did not reach the affected portion of the lung. Here was a suggestion of another circulatory abnormality which merits further attention.

SUMMARY

Reduction of blood volume, mainly of plasma volume, was fairly common in severe peritonitis. A reduction of 20–30% of normal values was found at the first estimation, usually before operation, in about half the cases of recovery and in a rather larger proportion of fatal cases.

Under treatment with intravenous non-protein fluid the plasma volume in cases of recovery rose to normal or above normal, though in some instances the cell volume continued to fall for some days. In fatal cases the normal volumes were usually not regained, and sometimes a further fall took place before death.

Changes in plasma volume were accompanied by parallel changes in total circulating plasma-protein and a proportionately greater fall in circulating plasma-albumin, the deficit of which persisted for 2 weeks or longer.

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There was no close correlation between volume changes and the concentration of blood constituents—e.g., hæmoglobin, plasma-proteins, and plasma-chlorides.

The main causes of the volume reductions were ileus and exudation of plasma into the peritoneal cavity. Changes in plasma colloid osmotic pressure played no important part. Extravasation of blood into the bowel during ileus may have been partly responsible for the fall in cell volume.

There was evidence that reduction of blood volume produced renal injury. Renal failure was sometimes an important cause of death.

In some cases the blood volume was very low shortly before death, and the terminal collapse of the circulation could be attributed to oligæmia alone. In others the blood volume was nearly normal, and some other factor, possibly bacterial intoxication, had destroyed the efficiency of the circulation.

We are indebted to Mr. W. H. Carnie for much valuable technical assistance, and to Mr. C. D. L. Cromar and Mrs. S. Konstam for help in certain cases. One of us (P. H. T.) held a Garden Research Fellowship of the University of Aberdeen and later a personal grant from the Medical Research Council, for which grateful acknowledgment is made. Expenses were in part defrayed by a grant from the Marnoch Memorial Fund.

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SEROLOGICAL EVIDENCE OF Q FEVER IN GREAT BRITAIN

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Q FEVER was the name given by Derrick (1937) to an acute febrile illness noted among slaughter-house workers in Brisbane, Queensland. The rickettsial ætiology of this condition, which was not unlike mild typhus, was subsequently demonstrated by Burnet and Freeman (1937), and the causal organism is now known as *Rickettsia burneti*. Despite the surprising discovery by Burnet and Freeman (1939) and Dyer (1939) that rickettsiæ isolated from ticks in Montana, U.S.A., by Davis and Cox (1938) were identical with Australian strains of *R. burneti*, it was assumed for some years that natural infection of man was confined to Australia. Investigations by Robbins et al. (1946) in Italy during the late war, however, led to the isolation of *R. burneti* from spectacular outbreaks of atypical pneumonia among British and American troops. Serological studies showed that Q fever also occurred as a sporadic disease, and was probably endemic, among civilians in parts of Italy. At the same time the disease was identified in Panama by Cheney and Geib (1946), and in the following year outbreaks originating in the United States were reported by Topping et al. (1947) and Shepard (1947). Recently Schulze (1947) has produced evidence of Q fever in Germany, and cases have been reported in Switzerland by Gsell (1948) and in Turkey by Payzin and Golem (1948).

Many of the recorded outbreaks have occurred among people in close contact with cattle, but the exact source of infection is unknown. Inhalation of infected tick excreta from the hides of cattle has been suggested, because several species of ticks are infected in nature. Cattle themselves acquire infection, as shown by the presence of rickettsial agglutinating and complement-fixing antibodies and by the demonstration of *R. burneti* in milk from a surprisingly high proportion of dairy cattle in endemic areas of Southern California (Huebner et al. 1948). Q fever usually presents as primary atypical pneumonia, with radiological changes in most cases, but the condition is often very mild.

Because of the widespread distribution of Q fever it was decided to look for this disease among patients with atypical pneumonia and similar acute respiratory illnesses in Great Britain. The ultimate diagnosis depends on the isolation of the causal rickettsiæ, but except in recognised outbreaks this is rarely possible. A satisfactory alternative is the detection of specific complement-fixing antibodies (Smadel 1948), and this technique was used in the present investigation.

MATERIALS AND METHODS

Specimens of serum from patients with atypical pneumonia have been sent to Cambridge from several sources: locally through clinical pathologists in hospitals in East Anglia, and from a wider area through Dr. F. O. MacCallum, at the Virus Reference Laboratory, Central Public Health Laboratory, Colindale. Most specimens were also examined for psittacosis antibody by Prof. S. P. Bedson, and for lymphocytic choriomeningitis antibody by Dr. MacCallum. All these sera were inactivated at 56°C for 30 min. before testing. Yolk-sac antigens for use in the complement-fixation tests were kindly sent by Dr. Herald Cox, of Lederle Laboratories, New York. An American antigen (Nine Mile strain) and an Italian antigen (Henzerling strain) were used; the latter contains both the known antigenic factors of *R. burneti* in equal amounts, and it is considered the more suitable for general diagnostic work. After preliminary titration of complement in the presence of the antigen for two hours at room temperature, the test was set up with serial dilutions of serum, 2 units of complement, and antigen. These mixtures and the usual controls of antigen and serum were allowed to stand overnight at 2°C and then for an hour at room temperature, before the hæmolytic system, consisting of 1% sheep cells and 3 units of hæmolysin, was added. After incubation for 30 min. at 37°C the tubes were centrifuged and degrees of fixation recorded.

RESULTS

Of 24 sporadic cases of atypical pneumonia so far investigated Q-fever complement-fixing antibodies have been found in sera from 3. The details are as follows:

Case 1.—A glider pilot, aged 29, came to the R.A.F. station, Oakington, from the R.A.F. station, Netheravon, two days before he first felt ill on April 1, 1948. At the onset and throughout his illness he complained of headache, anorexia, and general malaise, but this was not accompanied by cough. Previous illnesses were measles in childhood and occasional attacks of bronchitis. He had been a prisoner in Germany for six months in 1943, during which he had remained well; otherwise he had never been abroad. After two days in the station sick quarters he was admitted on April 5 to the R.A.F. Hospital, Ely, where examination revealed a temperature of 99·8°F and adventitious sounds at the base of the right lung. His symptoms had gone and his fever had subsided by April 7, but on April 8 radiography revealed "right posterior basic segmental atypical pneumonia" (report by Flight-Lieutenant G. du Boulay). By April 15, however, further X-ray examination showed almost complete resolution. On April 8 the total leucocyte-count was 6800 cells per c.mm. (neutrophils 51%); no cold agglutinins were detected (report by Squadron-Leader W. T. Beswick). After a convalescence interrupted by a mild streptococcal tonsillitis the patient was discharged to sick leave on April 26.

The results of complement-fixation tests with Q-fever antigens are shown in the accompanying table. Samples of the first and second specimens were also sent to the

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COMPLEMENT-FIXATION TESTS WITH Q-FEVER ANTIGENS*

Case no.	Days since onset	Serum dilutions						Serum control 1/10	Antigen control
		1/10	1/20	1/40	1/80	1/160	1/320		
1	15	4	4	4	2	0	0	0	0
	33	4	4	4	4	2	0	0	..
	76	4	4	4	3	0	0	0	..
2	138	4	4	4	4	2	0	0	..
3	11	4	3	1	0	0	0	0	..
	72	4	2	0	0	0	0	0	..

4, complete fixation.
3, 2, 1, degrees of partial fixation.
0, no fixation.
* The same results were obtained with both Henzerling and Nine Mile antigens.

Army Medical School at Washington, where Dr. Ross Gauld kindly confirmed the results. Q-fever antibodies were present in significant titre, but this patient had spent six months in Germany, and, though he remained well, it was impossible to prove that the antibodies were not the result of a mild attack in that country. Nevertheless, the illness described had probably originated at Netheravon, where the patient had been stationed during the preceding months. Accordingly, inquiries were kindly made by Air Commodore J. M. Kilpatrick, Director of Hygiene, into the history of atypical pneumonia and similar illnesses at Netheravon during the early part of 1948. There were two possible cases, and it was practicable to investigate one only.

Case 2.—An aircraftman telephonist, aged 20, who remembered no previous illness and had never been overseas, first felt pain in the right lower chest on the evening of Feb. 25, 1948. This he attributed to a fall he had had earlier in the day. He was admitted to the station sick quarters, and on the following morning his temperature was 103°F and pulse-rate 100 per min. Slight dullness was present and adventitious sounds were heard at the base of the right lung. The patient was treated with sulphathiazole, and, though his general condition improved in two days, the temperature remained between 100 and 102°F. On Feb. 28 'Sulphamezathine' was substituted for sulphathiazole, still without effect on the fever, and on March 2, with a tentative diagnosis of virus pneumonia, the patient was transferred to the R.A.F. Hospital at Wroughton. Almost immediately the fever subsided, but it was noted on admission that, in addition to residual fine crepitations at the base of the lung, the spleen was easily palpable an inch below the costal margin. On March 4 this and all other abnormal signs had disappeared and radiography of the chest revealed no abnormalities. The total leucocyte-count at this stage was 7400 per c.mm. (neutrophils 68%). The patient was discharged on March 15.

A specimen of serum was taken on July 7, nearly five months after the illness, and the result of a complement-fixation test is shown in the table. Samples of this serum were also sent to America, where Dr. Herald Cox kindly checked the results. The titre of Q-fever complement-fixing antibodies was 1 : 80, which is highly significant six months after the illness. The patient had never been overseas, and it seems probable that he had been infected with Q fever contracted in this country.

The third case was unconnected with the first two and was brought to notice by Dr. Stark Murray, pathologist to Kingston County Hospital, through the Virus Reference Laboratory at Colindale.

Case 3.—A builder's labourer, aged 76, was admitted to Kingston County Hospital on June 25, 1948, with cough and pain in the right side of his chest for one day. He could recall no previous illness except "gastric trouble," and he had never been overseas. Examination revealed a temperature of 100·6°F and signs of right-sided pneumonia. The patient was accordingly treated with sulphamezathine, and next day his symptoms had gone. Fever and signs of consolidation of the right lung persisted, however, and were confirmed by radiography on June 28. His white-cell count was 6000 per c.mm. (neutrophils 54%) on June 30, tubercle bacilli were not found in the sputum, and a test for cold agglutinins was negative. The fever subsided on July 1, the consolidation resolved, and the patient was discharged on July 10.

Specimens of serum were received on the 11th and 72nd days of illness, and on each occasion Q-fever complement-fixing antibodies were present at a dilution of 1 : 20. Though titres of 1 : 10 or higher are generally taken as evidence of infection with *R. burneti* at some time in the past, a titre of 1 : 20 soon after the disease is more difficult to interpret. Thus the diagnosis of Q fever cannot be made with certainty in this case. Since rickettsial complement-fixing antibodies persist for long periods, it is always possible that these patients had been infected with Q fever much earlier than the illnesses described; nevertheless, two patients must still have been infected in this country. Neither psittacosis nor lymphocytic choriomeningitis antibodies were found in sera from cases 1 and 2. Serum from case 3 was only examined for psittacosis antibody, and this was not detected.

If, as this evidence suggests, Q fever occurs in Great Britain, the diagnosis should be considered in localised outbreaks of acute respiratory illness as well as in sporadic cases of atypical pneumonia. Studies of such outbreaks are more likely to provide final proof, the isolation of *R. burneti*.

SUMMARY

During an investigation of atypical pneumonia in Great Britain Q-fever complement-fixing antibodies were detected in serum from 3 of 24 patients examined. Two of these patients had never been overseas, and this is regarded as evidence that Q fever occurs in the British Isles.

Thanks are due to all those mentioned in the text. Permission for the publication of cases 1 and 2 has been obtained from the Air Ministry.

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". . . It is the experience of everyone connected with medicine today that training received while in school or as an intern is much farther advanced in the fields of specialisation than it is in practical experience. This is an unfortunate and evil result of the unparalleled progress in technology that came about in the last generation. . . . We see in print so often that what is needed is the formation of a specialty in general practice, that the general practitioner should be integrated into this or that group, that he should be supervised, that he should realise his limitation, that he should have this or that internship, that he should be glorified, that he practises the broadest specialty in medicine, etc., etc., ad infinitum. What is really needed is that the educational administrator of our medical school and the medical staff of our hospital recognises that the student and intern needs a balanced diet instead of an indigestible assortment of courses selected and arranged by the specialist. . . ."—*General Practice News*. Quoted from *Public Health Economics*, October, 1948, p. 516.

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STREPTOMYCIN IN WHOOPING-COUGH

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THE sensitivity of gram-negative bacilli to streptomycin has been reported by many workers. Strains of *H. influenzæ* isolated from cases of meningitis have proved sensitive to 0·8–10·8 units of streptomycin per ml. (Logan and Herrell 1946, Alexander 1946, Birmingham et al. 1946), and strains of *H. pertussis* 3–5 units per ml. (Hegarty et al. 1945, Alexander 1946). The protective power of streptomycin against *H. pertussis* was tested by Bradford and Day (1945) and Hegarty et al. (1945) in mice. Complete protection was not obtained, but judged by length of survival and by lung cultures, the treated mice appeared to benefit somewhat.

In the hope that streptomycin would prove lethal to *H. pertussis* and *H. parapertussis* in man, a clinical trial was undertaken.

LABORATORY TECHNIQUES

Blood-streptomycin Assay

Serum from patients treated by inhalation and from cases 13 and 14 (tables II and III) receiving intramuscular streptomycin was assayed by the technique described by May et al. (1947). Staphylococcus "Mayo Clinic" was the test organism used. All the sera were inactivated. A standard curve was made for each assay.

Serum from cases 8 and 11 (tables II and III), treated with intramuscular streptomycin, was assayed by Mitchison and Spicer's (1949) technique; 10 cm. lengths of glass tubing 2 mm. in internal diameter were used. One end was sealed with 'Plasticine.' 20 ml. assay agar (Stebbins and Robinson 1945) was inoculated with an overnight culture of *Staph. mayo* in broth to give a final concentration of 1 in 1000. The agar-staph. suspension was left at 52°C while the 8 cm. columns were pipetted into the tubes. When the medium had set, a 1 cm. column of patient's undiluted serum was layered on to the medium. Four tubes were inoculated for each assay. A control series, ranging from 100 units to 0·75 unit of streptomycin, was set up from each bottle of 20 ml. assay agar. Here again four tubes were used for each standard.

The tubes were incubated overnight, after which the column of agar free from staphylococcal growth (from the concave agar meniscus to the line of colonies) was measured under a dissecting microscope. A graph was plotted, the ordinates representing the column of inhibition in mm., and the abscissæ the log of the streptomycin in units. A straight line resulted, from which the patient's blood-streptomycin level could be deduced. The fewness of the manipulations, the speed with which agar can be layered on the agar column, and the great range of values accessible for an end-point on the graph are valuable factors in this technique. At the lower levels of streptomycin determinations the accuracy obtainable was considerable.

Urinary Assay

The urine was tested for alkalinity, and dilutions were prepared from 1 in 10 to 1 in 5120, using 0·5% glucose broth on the alkaline side of neutrality, with methyl-red indicator. Two drops of 1 in 1000 overnight culture of *Staph. mayo* were placed in each tube. After overnight incubation the end-point was noted. A control series starting with 10 units of streptomycin per ml. in glucose broth was set up with each test.

In-vitro Sensitivity of H. pertussis and H. parapertussis to Streptomycin

The strains usually reached their greatest growth after 72 hours at 37°C in an atmosphere of air containing 5% carbon dioxide. Great difficulty was experienced in obtaining a reliable Bordet-Gengou medium. The base, containing 4% nutrient agar and glycerinated potato extract, was supplied by the London County Council. Either the blood was collected from cases of heart-failure and defibrinated, or outdated blood was chosen from the transfusion bank. The supernatant serum or plasma having been aspirated down to the waist of the transfusion bottle, the blood was added to the base in the proportion of 1 to 3. Provided the plate was used the same day as it was poured and dried, or used after having rested 18 hours on the bench, it was easy to inoculate. Plates stored in the ice-chest became soft, and dark patches of altered blood appeared. After first subculture the strain usually became well established. However, on occasions plates did not support growth or became covered with fungal growth within 48 hours' incubation. The primary culture was inoculated on Bordet-Gengou and on 50% serum-agar medium and tested against pertussis and parapertussis antisera. No strains of *H. parapertussis* were isolated.

Sensitivity to streptomycin was tested on three separate occasions by incorporating the antibiotic in the Bordet-Gengou medium. The calculated quantity of streptomycin was added to the base before the addition of blood and poured immediately. The 10 strains isolated from the present series, 8 strains received from the Lister Institute (G 527, G 534, G 463, G 491, G 430, H 2359, H 2361, and H 2362), and 1 strain from Oxford (JG 580) were tested. Six strains were inhibited by 4 units, and the remaining 13 strains by 2 units of streptomycin per ml. *H. parapertussis* (CR_2), from Colindale, grew on a plate incorporating 8 units of streptomycin per ml. The plates were incubated for 6 days.

Alexander (1946) gives a figure of 3–5 units per ml. for the streptomycin sensitivity of *H. pertussis*. He gives no data of the technique used for this estimation. Hegarty et al. (1945), incorporating streptomycin in Bordet-Gengou and in Hornibrook's medium, obtained growth with concentrations of 3 units per ml. and no growth with 6 units per ml. They worked with four strains of *H. pertussis*. These workers demonstrated the bactericidal action of streptomycin by inoculating a heavy suspension of *H. pertussis* in Hornibrook's medium containing 18 units of streptomycin per ml. Subculture made at regular intervals showed that, after 30 hours, 99·75% of the organisms were non-viable.

It appears desirable that clinically the blood-streptomycin level should be maintained at 2–8 units per ml.

Complement-fixation Test

Rabbit antisera were prepared by intravenous inoculation with a growth of hæmophilus which had been washed off a Bordet-Gengou plate and killed in 0·25% formol saline solution. After 6 weeks parapertussis antiserum yielded a titre of 1 : 2500, and pertussis antiserum 1 : 1250.

The antigen was prepared from 4-day-old growth on Bordet-Gengou medium. With a bent glass rod the culture was harvested in 0·25% formol saline solution. The pooled deposit from twelve plates was ground in a Griffith's tube, resuspended in formol saline solution, and gently centrifuged until the supernatant fluid matched in opacity a suspension of 8000×10^6 *Bact. coli* per ml. The antigen was titrated by incubating equal volumes of antiserum, complement (3 M.H.D.), and antigen of varying concentration ($0{\cdot}5 \times 10^6$ to 8000×10^6 organisms per ml.) at 37°C for an hour. To this series two volumes of sensitised sheep red cells were added and fixation of complement noted. Pertussis antiserum fixed complement when the pertussis antigen was used in a concentration of 1000×10^6 or 500×10^6 organisms per ml. This serum did not fix complement when parapertussis suspensions were used. Parapertussis antiserum fixed complement when parapertussis antigen suspension contained 500×10^6 organisms per ml. and did not show fixation with pertussis suspensions. The antigen suspensions were therefore always made to contain 500×10^6 organisms per ml.

The patients' sera were inactivated and put up against the two antigens so that the final dilution was 1 in 3. Any sera which possessed antibody were further titrated in final dilutions of 7·5, 15, 30, and 60. The control rabbit's serum, tested on five occasions, yielded a titre of +15−. None of the 11 patients examined during their 10th to 12th week of illness exceeded this figure, and all fixed the strain of *H. pertussis* and not the *H. parapertussis*.

Blood-counts

The normal standard of blood-counts for children (table I) was taken from Still (1927). It will be seen in table II that the first 5 cases fell well within normal limits and therefore correlated well with the early stage of infection. During the second week of infection 5 out of 6 cases showed a definite leucocytosis, with a relative and absolute lymphocytosis. The highest counts with predominant lymphocytosis (except

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in case 13) were obtained in the 3rd and 4th weeks. Donald (1938), reviewing the counts of 123 cases, found that the relative lymphocytosis persisted during the 9th and 10th week in half his cases.

ORGANISATION OF CLINICAL TEST

The Medical Officer of Health and local practitioners notified the laboratory as soon as they saw a suspected case of whooping-cough. The pathologist visited the patient and took a nasopharyngeal swab, which was

TABLE I—NORMAL WHITE-CELL COUNTS IN CHILDREN

—	At birth	6 mos.	2 yr.	5 yr.	10 yr.
Total leucocytes per c.mm.	24,000 to 62,000	15,000	13,000	11,000	9000
Lymphocytes %	20–22	57	52	37	32

plated on Bordet-Gengou medium (33·3% human blood) which had been flooded with a solution containing 15 units of penicillin per ml. (Cruickshank 1944). To avoid delay, treatment was started before the cultural confirmation was obtained. The patients were conveyed twice a day to a cubicle in the hospital for inhalation of streptomycin 150,000 units: 11 children were treated in this way; 3 others were warded and inhaled streptomycin 150,000 units four times a day, 1 of them (case 13) receiving also intramuscular streptomycin 200,000 units four times a day; and 3 others were given intramuscular streptomycin 200,000 units four times a day.

The parents had explained to them the experimental nature of the investigation; but, because of the distress of the children, the parents (except in 2 cases) expressed disappointment and even resentment at the frustration of their hopes. It needed "personal" persuasion to obtain blood for the final complement-fixation test. Two neighbouring families refused because "the children still had spasms when excited."

Streptomycin hydrochloride (Merck) was used throughout: 1 g. was dissolved in sterile distilled water to yield 50,000 units per ml. This stock solution was kept at 0°C. The quantity required for each patient was poured into the Collison container. Potency tests of the stock solution proved that it was unimpaired after 5 months at 0°C. Aeration for 30 min. with oxygen did not lower its streptomycin content.

We based our dosage of 50,000 units per ml. for volatilisation on the work of Heilman et al. (1945), who found that 50,000 units per ml. did not irritate the mucosa of the tracheobronchial tree in three adults with tuberculosis. Two of their patients, on 500,000 units per 24 hours, did not yield estimable levels of streptomycin in blood and urine. The third patient, however, on the same dosage, who could hold a deep inspiration for 5 min. at a time, had 30,000 units in the 24-hour specimen of urine. Figi et al. (1946) reported that a patient with laryngeal tuberculosis was successfully treated by inhalation of streptomycin 50,000 units at the beginning of each hour for 10 hours a day for 6 weeks and streptomycin 0·8–1 g. a day by intramuscular injection.

Ample warnings of the risks of toxic manifestations have been published. The *British Medical Journal* (1947) gives a detailed review of their seriousness. Eighth-nerve deafness, in a significant number of patients treated for longer than a week, makes it a very real responsibility to determine and use the shortest effective period of treatment. Alexander (1946) found that the treatment could be shortened to 5 days for most of his cases of *H. influenzæ* meningitis. We therefore limited our trials to 4-day periods.

INHALATION THERAPY

A baby's gas helmet (see figure) was fixed to the iron bars of a cot with a retort clamp. The inlet aperture was connected to the Collison aerosol volatiliser. With the baby on its mother's knee, the helmet was lowered over the child, so that it could see through the transparent window with comfort. The hood was loosely tied below the child's arms and waist. While the machine was working, a cloud of streptomycin and oxygen escaped from beneath the hood. Each patient was left under the helmet for 10 min. and, with the machine "full on," 3 ml. of the material containing 50,000 units streptomycin per ml. was discharged. Older children sat on chairs; none of the patients seemed uncomfortable or frightened.

Investigations.—From each patient, after the first inhalation, a sample of blood was taken at 15 and at 60 min. From 2 warded and 2 visiting patients the streptomycin content of urine collected after the 1st hour and after 24 hours of inhalation was assayed. Neither in blood nor in urine was streptomycin detected. None of the children expectorated, so the streptomycin levels in the sputum could not be investigated.

A total and differential white-cell count was made in every case (table II).

Results.—Mothers and nurses were asked to record on paper the number of the patient's cough spasms during each 24 hours. These figures were used as a measure of improvement. The cases were visited during the 1st, 2nd, and 8th week after hospital treatment.

Apparatus used for streptomycin-inhalation therapy.

Of the 9 patients in the catarrhal stage 2, brother and sister contacts of a case in the same house, never developed whooping-cough. The strain isolated from one of them was identified on morphological and colonial appearance only, for subcultures were lost owing to plate contaminants, thus preventing agglutination tests from being carried out. The other 7 cases first treated in the catarrhal stage all developed typical whooping-cough with bouts of vomiting.

None of the recorded toxic symptoms were encountered, but 1 patient developed "ear trouble," which responded to sulphonamide therapy, and case 13 developed pneumonia.

INTRAMUSCULAR THERAPY

The mothers did not object when streptomycin inhalation therapy was offered, but consent was withheld when they realised that the child was to be "pricked." It was therefore decided to limit the intramuscular injections to four 4-hourly injections in the day-time and not to inject the children in the night, the whole course to be completed in 4 days.

Case 8.—A girl, aged 6 years, was afebrile, irritable, and having about 4 spasms of coughing during the day-time and 3 at night. She received 200,000 units intramuscularly in 0·5 ml. 4-hourly for 4 days, and on the 5th day a single intramuscular injection of 500,000 units was given to ascertain the peak blood-concentration. Table III records that the larger injection did not appreciably raise the blood-streptomycin levels. A total white-cell count of 14,500 per c.mm.

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and nasopharyngeal cultures confirmed the diagnosis of whooping-cough.

Result.—When visited at home two weeks later, the child only "whooped" when the weather was cold or wet. After 8 weeks she had completely recovered.

Case 11.—A girl, aged 2 years, sister to case 8, was less ill but always had spasms of cough when blood was being taken. Treatment and results were similar to those in case 8. The low figure for urinary streptomycin was due to the small quantity collected free from fæcal material. When seen after 8 weeks the child was still whooping but looked well and was gaining weight.

Case 13.—A girl, aged 3 years, received intramuscular streptomycin 200,000 units in 0·5 ml. 4-hourly during the daytime for 4 days. Directly after each injection she inhaled 150,000 units. The blood-levels (table III) began to decline after the 2nd hour. Urine secreted during the 1st hour after injection contained 3000 units per ml. Owing to the urine lost during defæcation, the streptomycin content of the 24-hour specimen is low. A total white-cell count of 51,000 per c.mm. bears out that this child was acutely ill. Cough plates grew *H. pertussis*.

Result.—The child was whimpering and febrile during the first 48 hours in hospital. There was a definite improvement on the 3rd day, when the temperature remained normal, but on the 4th day she became very listless. Contrary to advice, the parents took the child home on the 5th day. Five days later she was admitted to the Watford Isolation Hospital with lobar pneumonia. She became severely ill, was treated on conservative lines for 4 weeks, and was discharged after 6 weeks.

Case 14.—A boy, aged $2^3/_4$ years, had been put to bed 23 days previously with a feverish cough, but when visited had been running about for 10 days with catarrh and spasms of coughing. A total white-cell count of 22,500 per c.mm. and a nasopharyngeal swab substantiated the diagnosis.

Result.—The night following the first four injections the mother recorded fewer but longer spasms; on the 3rd night she was awakened once. However, when visited a week later, the child was still having 6 or 7 spasms a day and was vomiting regularly after the midday meal.

CONCLUSION ON RESULTS

The streptomycin therapy which we used had entirely negative results. The clinical course of the whooping-cough progressed unmodified. The early contacts developed the disease, those who had whooped before treatment had their expected period of illness, and in those cases where the disease was well established there was no apparent benefit.

TABLE III—STREPTOMYCIN LEVELS IN BLOOD AND URINE AFTER INTRAMUSCULAR ADMINISTRATION

Case no.	Dose given four times a day for 4 days (units)	Day of treatment when assay made	Blood-levels (units/ml.) after 1 hr.	2 hr.	3 hr.	4 hr.	5 hr.	Urinary levels (units/ml.) after 1 hr.	In 24-hr. specimen
8	200,000	2nd	..	15	..	..	7	..	..
		4th	..	16	5	..	2	..	1280
	500,000 units I.M. single dose	5th	..	32	22	..	6	..	..
11	200,000	2nd	..	..	19	..	8	..	..
		4th	..	23	17	..	5	..	160
	500,000 units I.M. single dose	5th	..	29	20	..	12	..	..
13	200,000 (plus 150,000 by inhalation)	2nd	16	12	12	8	..	3000*	80
		4th	32	32	16	16	8	..	..
14	200,000	2nd	32	32	16	16	4	640	320

* After 18 hr. level was 3 units/ml.

DISCUSSION

To ascertain whether the apparatus (see figure) nebulised material successfully, one of us inhaled 3 ml. of penicillin 50,000 per ml. for 10 min. Blood titrated an hour later contained penicillin 0·04 unit per ml.

Knott and Clark (1945) record a similar test. One of these workers remained for 15 min. in a room of 3000 c. ft. capacity which had been filled with penicillin mist from a Collison apparatus. The machine had nebulised 20 ml. of penicillin 10,000 units per ml. An hour later the urine and blood inhibited the test organism in dilutions of 1 in 2 and 1 in 3. Barach et al. (1945), Oslen and Clagett (1945), and Hagens et al. (1945), using modified inhalers, found similar blood-penicillin levels in patients who had inhaled 20,000 units.

TABLE II—CLINICAL AND LABORATORY FINDINGS IN THE SERIES

Case	Sex	Age in yr.	At start of treatment: Clinical stage	Estimated duration of illness (days)	Duration of whoop (days)	Total white cells per c.mm.	Lymphocytes %	Streptomycin route and dosage (units/24 hr.)	Bacteriologically proved	C-F test titres after weeks of infection: 4–7	10–12
1	F	14	C	1	..	8,900	43	A 300,000	–	3	..
2	M	4	C	7	..	12,200	40	A 300,000	? +	<3	3
3	F	2	C	7	..	10,000	42	A 300,000	–	<3	3
4	F	$^6/_{12}$	C	< 7	..	9,000	69	A 300,000	+	<3	+15 +
5	M	$^3/_{12}$	C	< 7	..	13,000	70	A 300,000	+	<3	..
6	F	5	C	7	..	10,000	73	A 300,000	+	<3	+15 –
7	F	$1^3/_4$	C	10	..	13,000	84	A 300,000	+	<3	..
8	F	6	C	21	..	14,500	73	IM 800,000	+	<3	+15 +
9	F	8	C	21	..	15,000	65	A 300,000	+	<3	..
10	F	5	EP	14	1	8,000	45	A 300,000	+	3	+15 –
11	F	$2^1/_2$	EP	14	1	21,000	67	IM 800,000	+	<3	7·5 +
12	M	7	EP	14	1	29,000	68	A 600,000	+	<3	+15 –
13	F	5	EP	7	1	51,000	83	{IM, A} 1,400,000	+	<3	+15 –
14	M	$2^3/_4$	EP	28	1	22,500	80	IM 800,000	–	<3	+15 +
15	F	$1^1/_2$	LP	28	14	14,700	62	A 300,000	–	3	..
16	F	3	LP	28	17	31,200	58	A 300,000	–	<3	+7·5 +
17	F	3	LP	28	21	20,200	40	A 600,000	–	3	..

C = Catarrhal. EP = Early paroxysmal. LP = Late paroxysmal. C-F = Complement-fixation. A = Aerosol. IM = Intramuscular.

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If penicillin reaches the alveoli, it would be supposed that streptomycin does likewise. The latter, however, apparently does not penetrate into the pulmonary capillaries, since none was found in the blood.

To determine whether mucin had an inactivating effect on streptomycin, preparations of gastric mucosa ('Biomucin') and gut mucosa ('Enteromucin') were tested; 1 g. of each preparation in 5 ml. saline was made up to contain 100 units of streptomycin per ml. This, together with a control saline solution containing streptomycin 100 units per ml., was left at 22°C for 18 hours. When tested by Mitchison's technique the mucin proved inactive towards streptomycin.*

The possibility arises that the molecule of streptomycin is too large to penetrate the alveloar epithelial barrier, or that it is inactivated within the cell. There is ample evidence of its sensitivity to pH variation.

It may be argued that the toxin of *H. pertussis* was well established before treatment began. In two instances this was definitely not so. Two patients were contacts, the last to succumb in a family of 3 children. They were free from cough spasms when submitted to streptomycin inhalation, but developed paroxysms within 6 days of the treatment.

Parenteral therapy yielded sustained blood-streptomycin levels high enough to be effective against the pathogen. It must therefore be conjectured that the treatment was inadequate either because of the development of resistant strains or because either the dosage of streptomycin or the length of treatment was insufficient.

Dr. J. Ungar, of Glaxo Laboratories, has found (personal communication) in experimental murine pertussis that infected mice given streptomycin for 2 days die on the 4th day, but mice given streptomycin for 6 days are completely protected. Bradford (1949) has found that nasopharyngeal swabs become negative after aerosol therapy and not after intramuscular therapy. This emphasises the desirability that if another group of children are subjected to streptomycin inhalation they should be treated for a period longer than that used in this investigation (4 days).

SUMMARY

Streptomycin was given in whooping-cough by aerosol nebulisation to 13 patients, by aerosol and intramuscular route to 1 patient, and by intramuscular route alone to 3 patients.

Blood-streptomycin levels and urinary assays are recorded.

In none of the 17 cases, whether in the catarrhal, early paroxysmal, or advanced paroxysmal stage, was streptomycin beneficial.

Strains of *H. pertussis* and *H. parapertussis* proved sensitive to streptomycin in vitro. Reasons are suggested for the failure of this clinical trial.

We wish to thank the Medical Research Council for supplying the streptomycin; the many doctors who contacted the laboratory, though we were unable to make use of all the clinical material offered; Mr. W. J. Fincham for his technical advice; and Mr. W. Michels for taking the photograph.

*Evidence has since been obtained that sputum and lung extract have an inhibitory effect on streptomycin (Schwabacher 1948).

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FATAL ANURIA AFTER USE OF MYANESIN IN ANÆSTHESIA

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IN view of the different opinions expressed concerning the effect of 'Myanesin' on the kidney the following case is of interest.

A builder, aged 45, was admitted to hospital with seventeen years' history of abdominal pain, for which he had undergone appendicectomy seven years ago. After full investigation, duodenal ulcer was now diagnosed and operation was recommended. The patient was a fit-looking and muscular man, with a blood-pressure of 140/75 mm. Hg, blood-urea 33 mg. per 100 ml., and urine normal to routine tests. The only extra-abdominal imperfections discovered were scattered rhonchi all over the chest and a hæmoglobin of 11·8 g. per 100 ml. (86% Haldane).

Operation.—A subtotal gastrectomy was performed, together with a cholecystectomy, since the gall-bladder also was found to be diseased.

Anæsthesia.—Premedication consisted of papaveretum gr. $^1/_3$ and hyoscine gr. $^1/_{150}$. Induction was with soluble thiopentone 0·7 g., followed by myanesin 17 ml., anæsthesia being first maintained with gas and oxygen and then changed to cyclopropane. Relaxation being inadequate, a further 9 ml. of myanesin was injected, and subsequently further doses of 9 ml. and 4 ml. were given. At no time were the respirations depressed. In spite of the large dosage of myanesin relaxation was only fairly satisfactory.

Postoperative Course.—Recovery from the anæsthetic was uneventful, but next day the signs in the chest were more definite, especially at the right base, and bronchopneumonia developed, which, however, subsided satisfactorily after the exhibition of 'Sulphamethazine' 13·5 g. Two days after operation, though the blood-pressure was maintained and the patient took 6 pints of glucose-saline per day, his urinary output had fallen to 25 oz. in 24 hours, containing only 3 g. of chloride (as NaCl) per litre; it subsequently became progressively less, and by the fourth day complete anuria was established. The last drop of urine to be tested contained about 1·5 g. of chloride (as NaCl) per litre. Abnormal pigmentation of the urine was not evident macroscopically. Death occurred on the fifth day after operation. Blood taken soon after death showed a blood-urea level of 300 mg. per 100 ml.

Necropsy.—The only findings of note were the large kidneys, with pale swollen œdematous cortices and relatively dark congested medullæ, the distended small intestine, and the slightly œdematous lungs.

Histology of Kidneys.—Microscopically, most of the cortical glomerular tufts were shrunken and bloodless, while the remainder were necrotic. The capsular spaces of all contained variable amounts of a finely granular material staining pink with Biebrich scarlet, and there was some desquamation and necrosis of the capsular epithelium. The proximal convoluted tubules were completely necrotic and appeared as distended spaces containing pink finely granular debris. Little or no cellular structure was discernible in them. The thin segments of the loops of Henle were rather less necrotic and contained debris consisting of coarser dark orange granules. The thick segments of the loops of Henle and the distal convoluted tubules were as completely necrotic as the proximal tubules and contained similar pink material. The collecting tubules showed partial necrosis, with shedding of cells into the lumina; many of these lumina also contained casts, consisting, in some tubules, of large brownish rounded

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bodies strongly resembling red blood-cells, and, in other tubules, of smaller reddish-brown granules. All these pigment bodies and granules, though giving a negative prussian-blue reaction for iron, gave a positive reaction for hæmoglobin by Lepehne's benzidine staining method.

There was a fair degree of interstitial œdema, and in some places the granular pigment was seen to have penetrated outside the wall of a small collecting tubule and evoked a slight fibroblastic response. Occasionally a potential tubulovenous anastomosis could be demonstrated where there was a small collection of blood among necrotic tubule cells. The vasa recta of the medulla were distended and well filled with blood. The juxtamedullary glomerular tufts showed a few intracapillary red blood-cells, but were only slightly less shrunken and degenerate than the cortical tufts.

DISCUSSION

The case was manifestly one of renal cortical failure ending in death from uræmia, but the exact ætiology of this failure is not certain. There is a strong likelihood that the essential factor was myanesin. Additional factors, however, must have played some part, since, though the dose of myanesin was large (39 ml.), Mallinson [1] has given up to 50 ml. without ill effect.

Two explanations of this probable action of myanesin of the kidneys may be offered: (1) a toxic effect on the more sensitive cortical arterioles, causing shunting of blood to the medulla, cortical ischæmia, and subsequent cortical necrosis; and (2) an intravascular hæmolytic action, followed by deposition of pigment in the renal tubules and interference with tubular function.

It is regretted that more investigations were not carried out, especially that no specimen of urine was examined either microscopically or spectroscopically on the two days following operation, while the kidneys were still functioning. But that the condition might be due to myanesin was not suggested until the case was reviewed after death.

Our thanks are due to Mr. H. Kidd, F.R.C.S., for permission to publish the notes of his case.

RESTRICTION OF THORACIC RESPIRATION AS AN AID TO ABDOMINAL PALPATION

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RIGIDITY of the abdominal muscles is a valuable sign, provided it is genuinely reflex and not voluntarily assumed by the patient. To ask him to relax his abdominal muscles seldom succeeds, and various alternative means of discouraging voluntary rigidity are in common use—e.g., distracting his attention by conversation, or asking him to breathe through the mouth. Raising the head and shoulders on a pillow flexes the spine slightly and so makes for abdominal relaxation, and placing a pillow behind the knees, as the patient is lying on his back, may also help, if the lower limbs are relaxed and comfortable.

1. Mallinson, F. B. *Lancet*, 1947, i, 98.

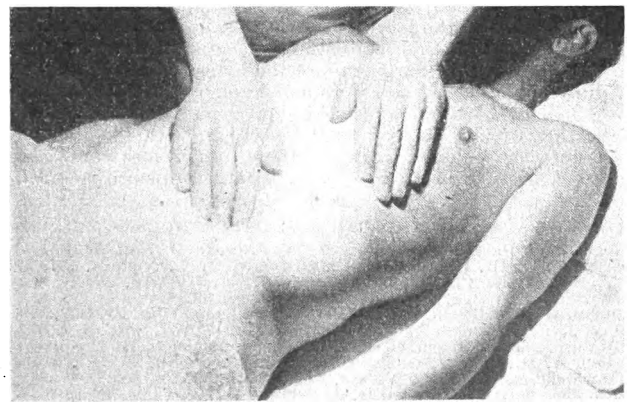

Fig. 1—One hand restricts thoracic respiration, causing relaxation of the abdominal wall, which is palpated by the other hand.

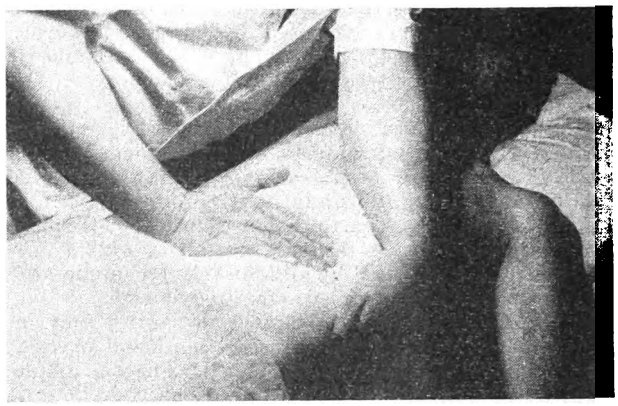

Fig. 3—Palpation of the left kidney: the right hand palpates the front of the kidney, in the usual way, while thoracic respiration is restricted by the left elbow; the back of the kidney is palpated by the fingers of the left hand in the renal angle with the left wrist in full ulnar deviation.

If the anterior abdominal muscles are contracted from reflex or voluntary causes, abdominal respiration is absent or much diminished and respiration becomes thoracic. Abdominal respiration cannot take place unless the anterior abdominal wall relaxes. The anterior abdominal wall will not relax if the rigidity is truly reflex, but if the abdominal rigidity is produced by a conscious effort it will usually disappear if thoracic respiration can be restricted, as has been previously shown.[1]

Thoracic respiration can be restricted in several ways. In ordinary abdominal palpation the examiner rests one of his palms on the patient's sternum and palpates the abdomen with his other hand (fig. 1). In some cases a fair amount of weight should be rested on the patient's sternum; in others the mere touch of the hand on the sternum is sufficient to change the character of the respirations.

The method is most useful perhaps in palpating and comparing the two iliac fossæ. For that purpose the patient lies on a trolley and the examiner stands behind the head of the trolley and leans over the patient till the examiner's chin and the patient's forehead are almost touching. The examiner rests his elbows on the

1. Nicholson, N. J. *Lancet*, 1938, i, 779.

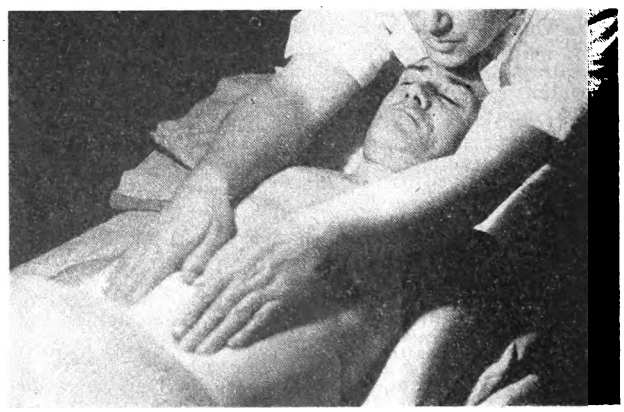

Fig. 2—The examiner's elbows restrict thoracic respiration, forcing the abdominal muscles to relax while the fingers palpate and compare the two iliac fossæ.

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front of the patient's thorax and so restricts thoracic respiration while his hands palpate the iliac fossæ (fig. 2).

To palpate the left kidney the examiner stands on the right of the recumbent patient and uses his right hand in the usual way to feel for the front of the kidney, while his left elbow rests on the patient's thorax. The examiner's left forearm is pronated, and his left hand, in full ulnar deviation at the wrist, creeps round the left side of the abdomen till the fingers reach the back of the kidney in the left renal angle (fig. 3). To palpate the right kidney this position is reversed.

In bimanual pelvic examinations abdominal relaxation may be improved if an assistant presses on the patient's chest.

POSTPARTUM HÆMORRHAGE FOLLOWING ECLAMPSIA

TREATED BY BLOOD-TRANSFUSION

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BLOOD-TRANSFUSION in eclampsia is always risky because of the renal condition, but in the following case it was imperative.

A primipara, aged 22, was admitted to hospital on Jan. 14, 1947, having had two eclamptic fits, seven and eight hours after spontaneous delivery of a full-time baby weighing 6 lb. 9 oz. in the presence of a very competent midwife before the arrival of the doctor. Labour had lasted 13 hours, but the second stage only 20 min., the cervix having passed from half to full dilatation within an hour. Delivery had been completed with an intact perineum and the spontaneous expulsion of a normal placenta with only slight loss of blood. Morphine gr. $^3/_8$ had been given, and the patient was admitted to Orsett Lodge Hospital three hours after the first fit.

Pregnancy had been complicated by pyelitis at the 18th week, the patient being confined to bed for 3 weeks on sulphonamide therapy. Otherwise antenatal findings had been normal and there was no history of previous renal disease.

On admission the patient was drowsy, with blood-pressure 145/100 mm. Hg, pulse-rate 100 per min., no œdema, a well-contracted uterus, and only slight bleeding per vaginam, which did not suggest any internal laceration. A catheter specimen showed a heavy cloud of albumin.

Treatment.—She was given morphine gr. $^1/_4$ three hours after admission, and chloral hydrate gr. 20 six-hourly for the next 24 hours, during which there were no further fits. After 36 hours there was a severe vaginal hæmorrhage of about 40 oz., patient being in a collapsed state with blood-pressure 90/60 mm. Hg and pulse-rate 120 per min. Before this a few large clots had been passed, but there had been no severe hæmorrhage.

Operation.—Under general anæsthesia an extensive left-sided tear of the cervix uteri was repaired with catgut and 1 pint of group-O compatible blood was transfused. This was followed by improvement in patient's general condition. Iron and ammonium citrate was given throughout her stay in hospital to combat the anæmia and, the hæmoglobin being still only 38% on the 14th day, a further transfusion of $^1/_2$ pint of group-O blood was given but had to be discontinued owing to a severe rigor.

Blood-urea level (see figure) rose steadily until the 8th day, after which it fell gradually to 33 mg. per 100 ml. on the 23rd day.

Urinary output (see figure) diminished to 8 oz. on the 4th day. To combat oliguria 1 pint of 4·285% sodium sulphate was given intravenously on the 3rd day. Fluid intake was restricted to about 30 oz. until one day the patient passed 110 oz. within 24 hours, whereupon the fluid intake was gradually increased.

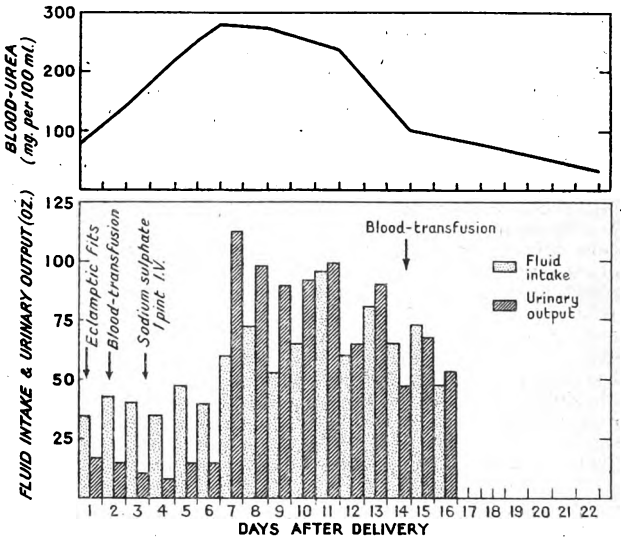
Urine contained a heavy cloud of albumin for several days but was practically clear before patient was discharged from hospital. At no time were any casts seen.

The *mental condition* remained remarkably clear during the first six days, but then the patient became confused and was difficult with feeding, and it was several days before she regained full mental acuity. The fundi oculi were normal throughout.

On the 23rd day, the patient was discharged to her home in good general condition, with blood-pressure 140/90 mm. Hg, blood-urea 33 mg. per 100 ml., and Hb 56%. Breast-feeding was not established, because of the mother's condition, but the baby did well on artificial feeds. On March 7, seven weeks after delivery, she came to the postnatal clinic in good health, with blood-pressure normal, Hb 80%, and blood-urea 22 mg. per 100 ml.

The delivery was described by the patient as quick and easy. During the first stage she had been walking about a good deal and the membranes had not ruptured early. The cervical tear may have been caused by the rapid last phase of dilatation and the rather precipitate delivery with a very short second stage. Probably the large doses of morphine contributed to the prevention of the earlier onset of severe hæmorrhage from the cervix.

The blood-urea level, which rose to 283 mg. per 100 ml. in the complete absence of casts in the urine, is an unusual feature. It did not fall very much for some days after



Blood-urea levels, fluid intake, and excretion of urine.

diuresis had started; hence the patient's mental confusion coincided with the highest blood-urea level. The severe postpartum hæmorrhage and consequent anæmia possibly helped to raise the blood-urea, but other factors must have been chiefly responsible.

I am grateful to Mr. L. Cosin, the medical superintendent, for permission to publish this case and for help with the text; to the other medical officers for their part in the treatment; to Mr. S. C. Phillips and his assistant for many laboratory tests; and to Sister Joseph and the nurses for their constant care with records; I am indebted to Dr. J. K. Farquharson and Nurse Bentley for their notes on the case before the patient came into hospital.

". . . The drift of the times, in the worlds of finance and industry, and in military policy, seems to be in the direction of the dogma of mass man. At their hands the individual is inevitably more or less depersonalised. Perhaps it cannot be otherwise, given the numbers of human beings involved and the complexity of most modern issues. . . . But the practising doctor and the parish minister are primarily concerned with individual human beings. The moment either begins to sacrifice his concern for the individual to some other hypothetical person, or to society in the abstract, he has mistaken his vocation."—Willard L. Sperry, *New Engl. J. Med.* 1948, **239**, 985.

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Reviews of Books

Reproduction and Survival

R. CHRISTIE BROWN, M.B., M.S., F.R.C.S., F.R.C.O.G., obstetric surgeon, City of London Maternity Hospital. London: E. Arnold. 1948. Pp. 108. 6s.

IN this little book some well-known biological facts about human and animal reproduction are restated, and the general theory of evolution summarised. There are chapters on the reaction of the embryo to its environment, on infertility and miscarriages, and on labour as an instrument of natural selection. Mr. Christie Brown makes the point that by superimposing an ethical process on the process of natural selection, man—and especially medical man—has created great problems for himself, since nature is concerned merely with the perpetuation of life, man with the saving of lives. He is content to state the position and does not attempt to offer a solution. The book should be useful to students of science and medicine and of interest to the intelligent layman.

Documenta Ophthalmologica

Editors: F. P. FISCHER, Utrecht; A. J. SCHAEFFER, Los Angeles; ARNOLD SORSBY, London. The Hague: Dr. W. Junk. 1948. Pp. 461. Fl. 36.

THE first volume of *Documenta Ophthalmologica* appeared in 1938. It was a collection of monographs, intended to fill a gap left by ophthalmic periodicals which mainly publish shorter communications. Publication has now been resumed with a larger editorial board.

The present volume contains seven contributions, two in French, two in German, and three in English. It also contains a tribute to the late Selig Hecht, who was on the editorial board of the first volume. The opening monograph by Tschermak-Seysenegg is a survey of physiological optics, incorporating much original work. The contributions by Gösta Karpe are the first tentative essays in the application of electroretinography to clinical work. Equally promising possibilities for clinical ophthalmology are indicated by R. Weekers and F. Roussel in their critical survey on the measurement of frequency of fusion. Poleff's review of experimental trachoma is a book on its own. The monograph by Bronkhorst, Ten Doesschate, and F. P. Fischer on the physiological optics of the visualisation of X-ray pictures, and that by Ten Doesschate and F. P. Fischer on the mechanical properties of the eye and its tissues, are further evidence of the high standard of this collection.

Die automatische, endogene, lymphaden-bronchogene Reinfektion in der initialen Periode der Tuberculose

Prof. PH. SCHWARTZ. *Folia Pathologica.* 1948, vol. I, pp. 172.

UNDER the title Folia Pathologica, and under the general editorship of Professor Schwartz, the institute of general pathology and pathological anatomy of the University of Istanbul proposes to issue a series of monographs recording the results achieved in the past fourteen years. As the subject of his first monograph Professor Schwartz has chosen endogenous bronchogenic lymph-gland reinfection in the initial stages of pulmonary tuberculosis.

He describes what he regards as a standard experiment: a rabbit is given an intratesticular immunising dose of tubercle bacilli of the human strain, and some weeks later an intratracheal or intravenous reinfecting dose of the bovine strain. In this way Schwartz obtains a reinfection type of lesion in the rabbit's lung which is the basis of his study of the progressive pulmonary tuberculosis of man, and which in his view is a fresh invasion of bacilli from the necrotic hilar lymph-glands of the primary complex. He discusses the various ways in which the invasion may take place: (1) massive caseous infiltration from the hilar glands; (2) radial spread along the chain of glands of the bronchial tree; (3) cavity formation by means of bronchogenic reinfection; (4) pleuritis, mediastinitis, and pericarditis from lymph-gland infection; (5) the early infiltration type of lesion—the *Früthinfiltrate* of German writers—which he regards also as a bronchogenic infection; and (6) reinfection from older tuberculous cavities.

These views are elaborated in a way that provokes thought, particularly at a time when the unsatisfactory terms "endogenous" and "exogenous" reinfection are under review. The monograph is beautifully illustrated with many photographs of the lungs depicting the various stages of the reinfection.

The 1948 Year Book of General Medicine (Chicago: Year Book Publishers. London: H. K. Lewis. 1948. Pp. 821. 25s.).—The viruses get a handsome showing this year from Prof. Paul Beeson, writing on infectious diseases. Prof. George R. Minot and Prof. William B. Castle review the year's work on diseases of the blood, blood-forming organs, and kidney, while Prof. Tinsley R. Harrison surveys diseases of the heart and blood-vessels, and Prof. George B. Eusterman deals concisely with the digestive system and metabolism.

Diseases of the Ear, Nose, and Throat (2nd ed. Bristol: J. Wright. 1948. Pp. 344. 25s.).—The second edition in Australia of this small textbook is accompanied by a printing in this country where it has apparently been in some demand. The author, Mr. D. G. Carruthers, of Sydney, writes clearly. Treatment with antibiotics is now included, and also—as is natural in an Australian work—a brief account of rubella deaf-mutism. The full description of tonsillectomy under local anæsthesia is presumably intended for "up-country" general practitioners who have to do such operations. The book should usefully instruct the undergraduate student and guide the general practitioner.

Clinical Electrocardiography (3rd ed. London: Heinemann Medical Books. 1948. Pp. 435. 30s.).—The new edition of this book by Prof. David Scherf and Prof. Linn J. Boyd, of New York, shows relatively few changes. The section on myocardial infarction has been considerably expanded but still occupies less space than the section on extrasystoles. Unipolar limb and chest leads are shortly considered, but their advantages, if any, are not brought out in the illustrations. Phonocardiography is not mentioned, though the development of this subject entitles readers to expect its inclusion in some form, however brief, in any work on cardiography. The cardiograms reproduced are adequate, though not profuse. The principles of cardiography are well set out, and should safeguard the reader from the common pitfalls in interpretation.

Minor Surgery (6th ed. Philadelphia and London: W. B. Saunders. 1948. Pp. 1058. 60s.).—The scope of this work by Prof. Frederick Christophers, of Chicago, is shown by the twenty-odd chapters, filling over a thousand pages, and by the fact that each chapter is followed by 400–500 references; its success is shown by the number of English-speaking surgeons to whom it is a familiar and trusty friend. The new edition is quite up to date, and the task of collecting and abstracting the innovations in minor surgery following the discovery of penicillin, and the innumerable war-time publications, must have been immense. Despite its size, the book does really confine itself almost entirely to the conditions with which a young house-surgeon may have to deal, and it gives explicit instructions about them. While all the chapters are sound, those on circulatory disturbances and preoperative and postoperative care are perhaps particularly impressive.

Radiology of Bones and Joints (4th ed. London: J. & A. Churchill. 1948. Pp. 700. 63s.).—This volume has now reached the proportions of an encyclopædia, and it is unlikely that any bone or joint abnormality, however rare, has escaped Dr. James Brailsford's eagle eye. Fourteen small-print pages of reference testify to his industry in this respect. "Encyclopædia" is the correct word, for it is not a textbook to be read at leisure. As a work of reference it has no equal in the English language, but its chief value lies in its analysis of world literature and in the careful descriptions of disease processes, based on Dr. Brailsford's wide experience. His tenacity in following up obscure cases over long periods is shown in many of the 615 illustrations. He rides one or two of his hobby-horses a little too hard: his aversion to biopsy of bone tumours could have been written less emphatically, and the section on spondylolisthesis, virtually amounting to a monograph on this rare condition, is perhaps out of balance. These, however, are minor faults in a first-class work.

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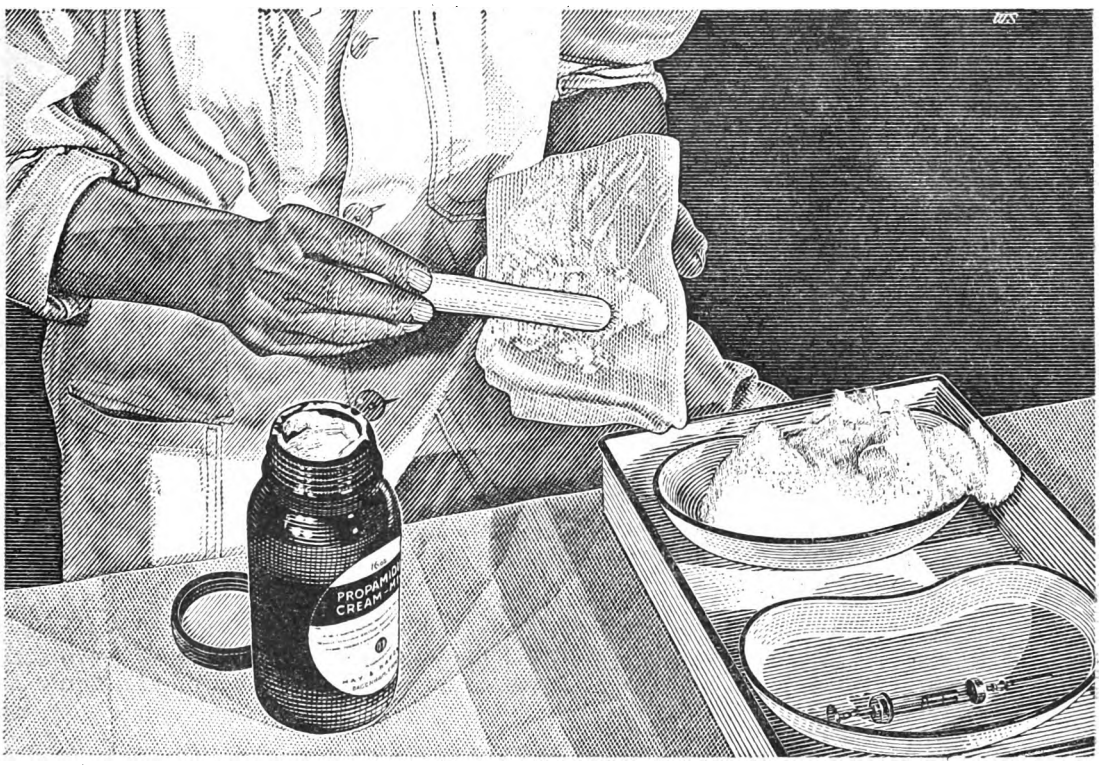

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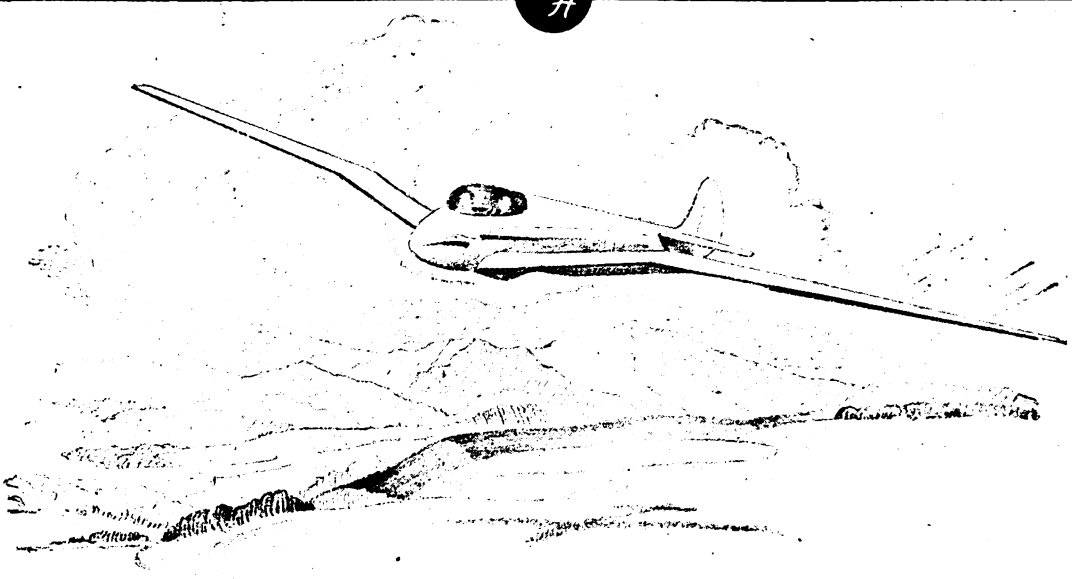

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THE LANCET

LONDON: SATURDAY, JAN. 29, 1949

The Capitation Fee

WITH six months' work completed, and two quarterly cheques received, the general practitioner can see more clearly how his future is shaping. Patients who intend to join a doctor's list have almost all done so; which means that most practices are likely to remain at about their present size. The initial period of novelty has passed, and (allowing for seasonal variations) there is little reason to expect any substantial change in the present load of work. So it is now possible to estimate both how busy and how lucrative a given practice is going to be. Almost all practitioners who make the comparison will report considerable alterations in their practices since July 5. For most there has been more work per patient—particularly for the women and the children—though not as much more work as many feared. Incomes have shifted in both directions. Some doctors with large practices in the most crowded urban areas find themselves with a larger income than they had before, but at the cost of heavy overwork. Others, in the more sparsely populated or more generously doctored areas, are shocked to see how small are the numbers on their list, how big is the fall in their incomes, and yet how busy their days remain. The net result of all this is a widespread conviction among practitioners that they are paid too little for the work they are asked to do, and urgent demands are being made for a review of the rates of remuneration.

Many of these demands suggest that all that is needed is an increase in the capitation fee. This, however, ignores the fact that the doctors hardest hit are those with the smallest numbers on their lists, who would be those least helped if the fee were simply raised. It is true that many of the smaller practices are in scattered rural communities, and that the hardship felt in such places will be appreciably diminished by recent increases made in the Mileage Fund. But small practices also exist elsewhere—in cities, in spas, in suburbs, and in seaside towns—where they will derive no benefit from this fund; and it is not easy to devise an equitable way of assisting them. One proposal is that a larger capitation fee should be paid in respect of patients who are over pensionable age, or who are chronic invalids, so that the spa or seaside practitioner (who claims to care for an abnormally high proportion of such people) would be more fairly remunerated. To do this would not in fact be administratively impossible; after all, something similar was done, though on a smaller scale, to allow extra money to be paid in respect of men invalided from the Forces; but it is doubtful whether it would provide a large enough subsidy to solve the problem for many of these areas with small practices. The Minister of Health has agreed that, in cases of proven hardship in such areas, application can be made for grants from the Special Inducement Fund; but doctors are showing themselves reluctant to take advantage of this largesse. The fund, of course, was originally intended to attract doctors to unpopular areas, and it is paradoxical that it should now be thought necessary to use it to enable doctors to remain in practice in "over-privileged" districts. And yet something must certainly be done; for the Act allows the established doctor the right to continue in practice in his own locality, and nobody wishes to see any doctor uprooted from a practice which he has long served and where he may be doing first-class work.

Another possibility, to which many are now returning, is a capitation fee that would vary in size according to the numbers on the doctor's list. It is suggested that if the first 1000 or 2000 patients were paid for at an appreciably higher rate than the remainder, many salutary results would follow. Such a device would bring immediate help to the doctor whose present list is, and now must remain, small; and such help can be justified by the fact that in small practices the expenses are as a rule relatively high, while the work demanded of the doctor per patient is often greater than in the numerically larger practices. Some excellent doctors cannot give a service satisfying to themselves or their patients if they make themselves responsible for more than a moderate number; and a graded capitation fee would enable these practitioners to keep to a manageable list without too much sacrifice of income. At present, moreover, serious difficulty is being experienced by young men and women who want to enter general practice. Few doctors feel themselves economically secure enough to justify their seeking extra help, and those that find such help essential apply for assistants rather than for partners; hence little security of tenure in practice is anywhere offered to the newcomer. A graded capitation fee—particularly if the increased capitation value were made payable on the list of a principal but not on that of an assistant—might smooth the way for the entry of more of these younger doctors into practice in those ill-doctored areas where their help is most needed. Moreover, if the grading of the capitation fee were sufficiently loaded, it could provide in itself all the advantages now claimed for the fixed annual payment, which might perhaps be discontinued—with all the controversy and dissension its distribution has so far caused. Among the present holders of long lists, a graded capitation fee might cause as much dissatisfaction as does the present support of the small lists by fixed annual payments subtracted from the total common pool. Undoubtedly it would do so if it meant an appreciable reduction in their present income. But if a new distribution scheme were negotiated as part of a general plan to give both higher and more equitable remuneration it should not be impossible to help the less fortunate

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low-list practitioners without penalising their busier colleagues.

All doctors in general practice hold that the total sum at present provided for their remuneration is insufficient; and time has demonstrably altered at least two of the factors on which it was calculated. The first of these factors is the number of doctors in the service: a sum intended to yield an adequate income for an expected service of less than 18,000 doctors is now shared between close on 20,000. The second is the betterment factor needed to translate the Spens proposals into present-day values: this stands at the low figure of 20%, which was laid down in 1946. An economist, who has been working on this problem at the request of the British Medical Association, argues that a betterment factor of 85–90% would be necessary if the increase were to allow fully for the changes in cost of the average middle-class budget between 1938 and 1948. A deputation has this week put a case to the Minister for allowing a much higher betterment figure. But if, as the profession earnestly and not unreasonably hopes, these representations result in more money being allotted to the Practitioners Fund, it will still be necessary to distribute that money in such a way as to give a fair reward to all for the differing types and amounts of work they undertake. We believe that serious consideration should be given to the graded capitation fee to see whether, in the present situation, it does not offer the wisest solution.

Kwashiorkor

LIKE many names in medicine, "kwashiorkor" has the merit of neutrality: it offers no explanation and its use prejudices no issue. It denotes a clinical picture whose essentials are dermatosis, lesions of mucocutaneous conjunctions, depigmentation of the skin and hair, diarrhœa, œdema, and fatty liver developing in infants or young children. At last week's meeting of the Royal Society of Tropical Medicine and Hygiene, Dr. H. C. TROWELL explained that he has abandoned the alternative title "infantile pellagra" because he believes that the rash, though pellagrous, is not necessarily a feature of the disease. He prefers the more comprehensive term "malignant malnutrition," which in his usage includes also kwashiorkor in older children and adults and cases with some but not all of the outstanding features of the syndrome.

Most workers now hold that the superficial lesions suggesting riboflavine and nicotinic-acid deficiency are only complications; they are not always present, and they may come or go overnight without other change in the severity of the condition. The œdema—which is associated with hypoproteinæmia—may be an expression of liver damage rather than the direct result of malnutrition; for BEATTIE and others[1] have shown that hypoproteinæmia is not the rule in famine œdema. The cause of the liver changes, which are sometimes irreversible, is still undecided. Fatty infiltration is constantly present, varying in degree with the severity of the illness.[2] DAVIES[3] has traced the sequence from the initial fatty infiltration through periportal fibrosis to diffuse cirrhosis of Laennec type. Many points, however, are still obscure. Is fibrosis the direct result of progressive infiltration? Is the cirrhosis in undernourished people a single pathological entity, or does it differ in different parts of the world? For instance, is the condition described by FERNANDO et al.[4] in Ceylon the same as that seen by DAVIES in East Africa? As to a remedy, WATERLOW[5] and the GILLMANS have shown that pure lipotropic factors such as methionine, choline, and inositol are of no value; and the GILLMANS' claim that desiccated stomach has a specific action has not been confirmed. TROWELL, like WATERLOW in the West Indies, CARVALHO[6] in Brazil, and ALTMANN[7] in Johannesburg, has obtained good results by treatment with milk alone. ALTMANN and MURRAY have reported that the anæmia also responds to milk, although refractory to iron and folic acid. This anæmia is typically normocytic and normochromic; but in East Africa macrocytosis is common, which led TROWELL to suggest that the cause might be a dual deficiency of iron and of the Wills factor. LEHMANN,[8] however, writing in these columns a fortnight ago, has shown that in such cases macrocytosis is a sign of regeneration after blood-loss from hookworm infection, and his work redirects attention to the part played by helminths and malaria in the general pattern of the syndrome. Here opinions differ, but there is no evidence that kwashiorkor in infants is anything but a nutritional deficiency disease. It is common in Johannesburg, where there is no malaria, and the cases described by WATERLOW in the West Indies were free of malaria and worms.

These studies in various parts of the world all indicate that the primary cause is protein deficiency. In fact ALTMANN and WATERLOW have remarked on the resemblance of kwashiorkor to the European *Mehlnährschaden* both in the clinical picture and in the history of feeding on a low-protein high-carbohydrate diet. In Africa kwashiorkor is often associated with vitamin deficiencies, for protein and vitamins of the B complex are distributed together in natural foods. The essential lesion may quite possibly be in the digestive system. BROWN and TROWELL[9] have demonstrated radiological abnormalities of the bowel pattern; WATERLOW has described atrophy and DAVIES fibrosis of the pancreas. CARVALHO[10] has obtained evidence of decreased pancreatic function, and the GILLMANS have drawn attention to changes in the salivary glands. If the organs most active in handling protein are also most vulnerable to protein deficiency, then the digestive tract and pancreas would be early sufferers: the intestine and pancreas have the highest protein turnover of any organs observed in tracer studies[11] and with fasting the pancreas loses the most weight. Grossman et al.[12] have found

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2. Gillman, J., Gillman, T. *Arch. Path.* 1945, 40, 239
3. Davies, J. N. P. *Lancet*, 1948, i, 317.
4. Fernando, P. B., Medonza, O. R., Rajasuriya, P. K. *Ibid*, 1948, ii, 205.
5. Waterlow, J. C. *Spec. Rep. Ser. med. Res. Coun., Lond.* 1948, no. 263.
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7. Altmann, A. *Clin. Proc.* 1948, 7, 32.
8. Lehmann, H. *Lancet*, Jan. 15, p. 90.
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11. Tarver, H., Schmidt, C. L. A. *J. biol. Chem.* 1942, 146, 69.
12. Grossman, M. I., Greegard, H., Ivy, A. C. *Amer. J. Physiol.* 1943, 138, 676.

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experimentally that the enzyme composition of pancreatic juice can be profoundly altered by changes in diet; while FRIEDMAN and FRIEDMAN [13] have produced pancreatic atrophy in rats on a low-protein diet. There is thus some experimental support for the possibility of a dietary lesion of the pancreas. This concept of an initial defect of digestion and adsorption would explain much—the complex clinical picture, the difficulty of treatment, and the tendency for a vicious circle to be set up.

Anticoagulants in Coronary Thrombosis

SUPPORT for the use of heparin and dicoumarol in the treatment of cardiac infarction has steadily grown in the ten years since SOLANDT and BEST [14] showed in these columns that heparin would prevent experimental coronary thrombosis and the resulting cardiac infarction. Today many American physicians contend that they should be given as a routine. At first enthusiasm was restrained because it was supposed that dicoumarol might cause dangerous hæmorrhages in the tissues generally and might aggravate bleeding into the wall of the coronary artery when this was a factor in coronary occlusion. Experience has shown that such untoward effects are rare and not of great importance. BLUMGART et al.[15] have investigated the effects of dicoumarol in dogs in which acute cardiac infarction had been produced experimentally. Half the animals received enough dicoumarol to keep the blood prothrombin at 12–20% of normal, while the other half served as controls. When the hearts were examined post mortem, no significant differences could be found between the two groups in the cardiac infarction, degree of necrosis, extent of hæmorrhage into the myocardium, or state of repair. It seems, therefore, that in dogs dicoumarol has no adverse effects on the myocardium which would retard healing or the development of a collateral circulation after cardiac infarction. Similar experimental results have been obtained by LEROY and NALEFSKI.[16]

In clinical cardiac infarction, anticoagulants might theoretically be useful in three ways—in preventing extension of the coronary thrombus or the development of fresh ones; in preventing the formation of thrombi in the cardiac cavities; and in preventing phlebothrombosis, which is liable to occur in an immobilised patient whose circulation is further slowed by the primary cardiac condition. MCCALL [17] gave dicoumarol to 71 patients with acute myocardial infarction; only 2 developed thrombo-embolism—1 a pulmonary embolus and the other an extension of the coronary thrombosis—and in both the reduction of prothrombin appeared to be adequate. REICH and EISENMENGER [18] used dicoumarol in 24 cases of acute cardiac infarction, and though 2 of their patients had a further coronary occlusion while under the treatment none had an embolic complication. They noted an undue sensitivity to the drug when cardiac failure was present. GREISMAN and MARCUS [19] found a great reduction of thrombo-embolism in a series of 75 cases of cardiac infarction on dicoumarol therapy, with an incidence of 4% as against 21% in controls not receiving the drug. In their view dicoumarol is particularly desirable in patients who are having digitalis, because this increases blood coagulability. On the other hand, dicoumarol is contra-indicated where there is liver insufficiency, any blood disease accompanied by a tendency to bleed, or ulcerative lesions of the gastro-intestinal tract.

WRIGHT and his colleagues [20] have collected reports from American hospitals covering 800 patients, rather more than half of whom were treated with dicoumarol (a small proportion with heparin also), the remainder being used as controls. The death-rate was 15% in the group having anticoagulants and 24% in the control group, the lower figure in the treated cases being largely accounted for by the lower incidence of thrombo-embolic complications. Most deaths occurred in the first two weeks of the illness, but there were a considerable number in the third and fourth weeks, suggesting that dicoumarol would be valuable even when begun after the first fortnight. They concluded that the duration of the treatment should be four weeks, either from the onset or from the latest thrombo-embolic accident. The greatest benefit from anticoagulant therapy was noted in the patients aged 60 or over. Apart from reducing mortality the drugs shortened the illness and reduced the risks of permanent disability, as from hemiplegia. Anticoagulant therapy clearly has an important part to play in the treatment of coronary thrombosis—if not in all cases, certainly in those that develop phlebothrombosis and always when embolism has occurred. All reports agree that it greatly reduces the incidence of venous and arterial embolism, but that it cannot prevent further coronary occlusion. Nor will it prevent ventricular rupture; whether it tends to promote such a complication is still uncertain. There are a few drawbacks to dicoumarol therapy; the necessary repeated prothrombin estimations are time-consuming and hæmorrhages do occur in spite of full precautions, though the risks from these are small compared with those of the complications which dicoumarol can prevent. Lately GIBSON [21] has suggested substituting salicylic acid for dicoumarol in coronary thrombosis. It is an old observation [22] that salicylates given for rheumatic fever sometimes cause mucosal hæmorrhages, and five years ago LINK and his colleagues in the U.S.A. showed that salicylic acid is a degradation product of dicoumarol and has a similar hypoprothrombinæmic action, also counteracted by vitamin K. There are therefore good experimental grounds for using salicylates—the American workers found aspirin more effective than salicylic acid—to reduce any thrombotic tendency there may be in patients with coronary thrombosis. It would also be interesting to know whether M. H. KNISELY [23] and his co-workers in Chicago, who have spent many years studying the "sludging" of blood in the conjunctival arterioles, have observed any sludge characteristic of the prethrombotic state which could be used as a reliable warning signal. For obviously the ideal time to give anticoagulants is before the first thrombosis.

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14. Solandt, D. Y., Best, C. H. *Lancet*, 1938, ii, 130.
15. Blumgart, H. L., Freedberg, A. S., Zoll, P. M., Lewis, H. D., Wessler, S. *Amer. Heart J.* 1948, 36, 13.
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17. McCall, M. *Amer. J. med. Sci.* 1948, 215, 612.
18. Reich, C., Eisenmenger, W. *Ibid*, p. 618.
19. Greisman, H., Marcus, R. M. *Amer. Heart J.* 1948, 36, 600.
20. Wright, I. S., Marple, C. D., Beck, D. F. *Ibid*, p. 801.
21. Gibson, P. *Lancet*, 1948, i, 965.
22. See annotation, *Ibid*, 1943, ii, 419.
23. See leading article, *Ibid*, 1948, i, 26.

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Annotations

THE MIDWIFE

NEARLY two years ago the Ministry of Health set up a Working Party, under the chairmanship of Mrs. Mary Stocks, principal of Westfield College, to inquire into the shortage of midwives and report on their recruitment and training. The members were Miss J. P. Ferlie, matron of the Simpson Memorial Maternity Pavilion, Edinburgh; Miss V. R. Shand, supervisor of midwives, Lancashire County Council; Mr. R. M. Titmuss, of the Cabinet Offices; and Dr. Albertine Winner, of the Ministry of Health. A steering committee included Dr. May Baird, of Aberdeen; Dr. W. S. Macdonald, of Leeds; and Mr. Arnold Walker, chairman of the Central Midwives Board.

In their report[1] the Working Party describe the midwife as "the practitioner of normal midwifery: the expert in normal child-bearing," and the partner and complement of the doctor in the midwifery service. A postscript expresses their disquiet at learning that some general practitioners giving maternity service under the National Health Service Act are taking over the whole of the antenatal care of patients and relegating midwives to the duties of maternity nurses. Sometimes midwives are not seeing patients until they go to deliver them; and some midwifery pupils are getting no opportunity to see antenatal care. This, the Working Party point out, is entirely contrary to the development of the maternity services intended by the Ministry of Health, and must react unfavourably on the recruitment of midwives. They hope to see the unwelcome trend quickly checked by administrative action. There are, in fact, indications that this trend is already correcting itself in some parts of the country, where practitioners are too busy to undertake work that can be done by midwives; but it could be renewed at any time. The doctor, the midwife, and the health visitor are a team who should work together; and the Working Party propose that the service should be reviewed in 3–5 years to ensure that the partnership is being maintained and that "there is no danger of the midwife being ousted from her proper place."

Notions about the "shortage" have changed greatly since 1929, when 14,479 midwives were thought to be "too numerous" to deal with 654,172 births (1 midwife to 45 births). Today 16,374 practising midwives for 688,270 births (1 midwife to 42 births) is held to be too few. The change is explained by the rise in standards of care: in 1929 antenatal care was sketchy, and the midwife left the patient 10 days after the birth of the baby. Nowadays much of the midwife's time is spent on antenatal visits, and she continues to attend the patient for 14 days after the birth—a period which the Working Party would like to see extended to a month.

Their chief recommendations relate to training. At present far more midwives qualify than practise; thus, in 1947 there were 74,219 names on the English Midwives' Roll, but only 17,095 had notified their intention to practise. It is wasteful to train large numbers of women who have no intention of practising; the Working Party urge authorities to consider carefully whether a midwifery qualification is essential when appointing candidates to nursing posts. It is also extravagant, and even undesirable, they think, to draw our pupil midwives largely from the ranks of trained nurses, as we do at present. The nurse is oriented to sickness and disordered function, whereas the midwife should be oriented to normal function and to health. Nevertheless, the midwife must be expert in nursing procedures; so they propose a new form of training—a basic course in general nursing, lasting $1^1/_2$–2 years, to be taken by entrants to both the nursing and the midwifery professions, followed by further training in midwifery or whatever branch of nursing is selected. During the basic course the student would have a month of carefully planned obstetric experience, which would enable her to discover and foster any latent taste for midwifery. The specialist training, taken at the end of the basic course, should, in their view, last a full year. Other recommendations are designed to improve the midwife's prospects of promotion, to raise her salary and status, to ensure that she has a car and adequate help at home, and to keep her work up to standard by refresher courses.

Women for all professions are drawn mainly from the secondary grammar schools, and there is a deficit of some 13,000 annually in the numbers of school-leavers available to meet estimated professional needs: on which the Working Party comment that a considerable proportion of the demand will have to be met from other sources of supply; that "if any profession has to go short the last to do so—for obvious reasons—should be midwifery"; and that facts of this kind should be closely studied by those anxious to promote overseas migration of large numbers of young people. As for other sources of supply, almost the only untapped source of woman-power remaining in this country are the middle-aged women, including widows and those whose children are past the early years. The Working Party believe that these could be persuaded to enter midwifery training in increasing numbers if their particular needs were considered. They might be trained in hospitals reserved for their own age-group, on lines that allowed for any greater difficulty experienced in learning after the 30th year is past, and they might well be non-resident during training. Here is another career for mothers, and a fitting one.

1. Report of the Working Party on Midwives. H.M. Stationery Office. Pp. 132. 2s. 6d.

SUPERSONIC AND ULTRASONIC

SOUND waves are periodic variations in the pressure of a material medium, not to be confused with the electromagnetic "spectrum," which extends from radio through ultraviolet radiations and X rays to cosmic rays, and can be transmitted through a vacuum. Sound waves above the upper threshold of perception by man were originally called "high frequency sonic waves" to avoid the oxymorons "silent sound" and "noiseless noise." Later they were called "supersonic" and still later "ultrasonic," but the arrival of jet aircraft led to confusion in these terms, so supersonic is now restricted to mean "faster than the speed of sound" (about 760 m.p.h.), whereas "ultrasonic" refers to high-frequency pressure (sound) waves. The upper threshold for the perception of sound by the human ear is about 20,000 vibrations per sec., though with ageing the threshold gradually falls. Many years ago Galton demonstrated with his whistle that dogs could hear sounds inaudible to man, and it has later been shown[1] that bats use ultrasonic emitting and receiving apparatus to avoid obstacles, as was suggested by Hartridge.[2]

Ultrasonic waves can be produced by making anything vibrate or pulsate at the appropriate frequency. This can be done mechanically or by the use of piezo-electricity or magnetostriction. Piezo-electricity means the production of an electric current by the compression of a crystal—e.g., quartz—and conversely the production

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2. Hartridge, H. *J. Physiol.* 1920, **54**, 54.

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of vibrations in a crystal by the application of an alternating electric current. An example of magneto-striction is the periodic contraction and expansion of a nickel rod in an alternating magnetic field. By some of these methods ultrasonic waves with a frequency of 12,000,000 per sec. can be formed. The uses to which ultrasonic waves have been put are extraordinarily various. Perhaps the best-known is the detection of submarines by ASDIC. The distance of an object could be measured by timing the echo from it; but a noise made so as to produce an echo from a submarine would be audible to the submarine's crew. The solution was to use ultrasonic waves, which the crew could not pick up unless they knew beforehand the frequency used. This method should not be confused with RADAR, which uses electromagnetic waves in a similar way. It was easy to adapt the ASDIC principle to mark hidden dangers to shipping and to give bearings secretly to war-time navigators. The principle has also been applied to industry, in the detection of flaws in metal and the level of a liquid hidden from view in a sealed tank.

The disturbance (cavitation) which ultrasonic waves create in their passage through a liquid medium has been put to many purposes. In 1923 J. R. Quain filed a provisional patent (no. 23921) relating to "the sterilisation of organic substances, whether in the form of liquids, semi-liquids, or solids, by means of impressing on them extremely rapid vibratory movement throughout their mass." Since then, suggested uses have included the destruction of bacteria,[3] viruses,[4] protozoa and infusoria,[5] yeasts,[6] and mosquito larvæ in the control of malaria[7]; the destruction of dirt in laundry work (but it is apt to damage the clothes also); the making of emulsions, especially for photography but also in the manufacture of cosmetics, paints, and food preparations such as "homogenised" milk, and the emulsification of fat for intravenous administration[8]; and the destruction of cerebral tissue[9] as a substitute for leucotomy without the need for craniotomy or other form of surgery (so far demonstrated only experimentally in dogs). The destruction of bacteria is performed not only for hygiene—e.g., sterilisation of milk—but also for the extraction of their antigens[10] and enzymes.[11] In a gas, ultrasonic vibrations will precipitate all solid impurities; in this way smoke and deleterious fumes can be abated, and fog dispersed perhaps more cheaply than with FIDO. The waves have been used in various ways in medicine—in deafness,[12] asthma,[13] and sciatica and other neuralgias,[14] and for the percutaneous administration of medicaments.[15] They have even been used as an aid in diagnosis.[16]

The energy of pressure (sound) waves is proportional to the square of their frequency, so the energy transmitted by ultrasonic waves can be enormous. Thus they will light a cigarette or boil a cup of tea at a distance[17] and have even been developed as a form of "death-ray." An ultrasonic gun devised in Austria in the late war was said to kill at a range of 65 yd. and to disable at 300 yd.

TEMPERATURE, PULSE, AND RESPIRATION

"THE charts at the end of the bed, tra-la, have nothing to do with the case."—So, in other words, sings a peripatetic correspondent on p. 199 of the familiar "T.P.R." records as logged by hospital nurses and orderlies, thus dragging into the light one of those time-honoured fictions about which we have all felt vaguely uncomfortable and which we have accustomed ourselves to respect as Sleeping Dogs and Let Lie.

Accurate temperature-taking, according to Vere Pearson,[18] calls for the retention of the thermometer for 2–5 minutes in the rectum or 15–20 minutes in the mouth (despite the manufacturer's assurance that the instrument is a $^1/_2$-minute affair). If each patient is to be closely supervised the while to see that he does not cheat, this means that one nurse will spend $2^1/_2$ hours getting round a ward of 30 mouth-takers and an hour to deal with 30 rectal experts. Obviously in these days of nurse-shortage some compromise is indicated. Is all this routine morning-and-night temperature-taking really necessary? Could it not be completely dropped in patients convalescent from accidents, operations, or self-limiting and apyrexial illnesses, once the danger-period of possible complications is past? Then the few pyrexial patients could enjoy accurate thermometry and the nurses would approach their lighter task with more interest and a greater zest for accuracy. Moncrieff and Hussey[19] have drawn timely attention to the pitfalls that beset the taking of infants' temperatures, and we can infer that it is more fruitful to note carefully the rectal temperatures of the few rather than to waste time wedging thermometers in the armpits of the many. Alternatively, the adult patient of average intelligence could surely have his own thermometer—a highly desirable precaution this[20]—and be taught to take and register his temperature at the statutory hours, as is the practice nowadays in most sanatoria. The few who might prefer to draw on their imaginations can usually be spotted beforehand. The argument that patients would then become temperature-conscious is fallacious: most patients can inspect their temperature charts and case-notes as it is, even though another medical fiction protests that they cannot.

Then, is pulse-taking necessary as a routine? It is open to abuses no less great though much less harmful than negligent temperature-taking. In a certain military hospital, so the story goes, only one of six nursing orderlies possessed a timepiece which was not away at the repairer's, yet all when taking pulses would stare gravely into an averted cupped hand before entering 72 or 80 according to taste on the charts; and no-one was any the worse. Accurate pulse-taking consumes time. Owing to the possibility of initial excitement, the first minute's score—though not without significance—may be positively misleading if recorded. Real counting, except of course during exercise-tolerance tests, should not begin until the pulse has settled down to a steady performance; which is sometimes as late as the third minute.

Finally there are the respirations, which in many hospitals are noted and recorded twice a day on all patients' charts regardless of the nature of their complaint. Is the "resting" respiration-rate often of any moment except in cardiac and pulmonary conditions, intracranial

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18. Vere Pearson, S. *Lancet*, 1909, ii, 852.
19. Moncrieff, A., Hussey, B. J. *Brit. med. J.* 1948, ii, 972.
20. Green, J. B. M., Penfold, J. B. *Lancet*, 1947, ii, 89. Albury, M. *Ibid*, p. 597.

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lesions, P.U.O., and hysteria? Can it be that it is still charted simply because there is a space for it on the printed chart which would look odd if left unfilled? May we urge that the goal of clinical records should be quality rather than quantity? If the time has not yet come for temperatures and pulse-rates to be recorded only at the special behest of the doctor in charge, at least let us agree that paper should no longer be wastefully soiled with imaginary graphs of the patients' respirations.

AUTORADIOGRAPHY

RADIOACTIVITY was discovered accidently by Becquerel in 1895, by means of what is now known as autoradiography, for he found that uranium ore left in contact with a photographic plate in the dark blackened the plate when it was developed. As a method of biological investigation, however, autoradiography was not much explored until a decade ago, when radioactive substances of biological importance began to be artificially produced in sufficient quantities. In 1924 Lacassagne and Lattes,[1] while investigating the distribution of naturally radioactive polonium in the tissues, had developed a method in which the histologist's paraffin block was pressed on a photographic plate. In 1940 Hamilton et al.[2] took up the task with radioactive iodine. They used paraffin sections of thyroid tissue, cleared in xylol and coated with a thin (1μ) film of celloidin, brought into contact with X-ray film by pressure. After suitable intervals the X-ray film was developed and fixed, and the tissue-section was stained in the usual way after dissolving off the celloidin. The autoradiograph and the section had to be compared later. Desirable improvements were the production of a single rather than a double preparation and an increase in resolution. The first of these presented fewer physical limitations than the second. Leblond[3] and Belanger and Leblond[4] have coated sections with melted photographic emulsions, through which, after the preparation has been developed and fixed, the sections can be stained with stains such as methylene-blue and Harris's hæmatoxylin. Endicott and Yagoda[5] and Evans[6] have mounted the sections directly on photographic plates and stained the sections after the plates had been developed.

The advantage of these methods is the intimate contact between section and emulsion; but from the cytologist's viewpoint their drawback is that the gelatin takes up most stains, obscuring somewhat the silver grains. Pelc[7] has used a stripping emulsion which is removed from its base for application to slides bearing sections; he too has had difficulty with the staining technique, and recommends viewing the sections by phase-microscopy. MacDonald et al.[8] also used stripping film, which for autoradiography is mounted emulsion side upwards on a section-bearing slide; for staining, the developed and fixed film and section is detached and remounted, emulsion side downwards, on another slide. Here staining can be perfect, but the section and photographic emulsion are separated by some 7μ of 'Cellophane' or its equivalent. Improvement of resolution depends on a number of physical factors. The radioactive atoms will emit either α or β particles. The α particle is fairly heavy, with a range in tissue of 20–40μ; the β particle is 7500 times lighter and thus for equal energy has a vastly greater velocity and range. Thus the probability of a β particle activating any silver grain it meets is much less than in the case of an α particle, which may be expected to produce a well-defined track in photographic emulsion. In fact about 10^7 β particles per sq. cm. are required to produce a useful blackening. The particles are emitted at random in all directions, and the atoms of the different radioactive substances have differing probabilities of undergoing their spontaneous change in unit time. Some of the factors to be considered, therefore, are: the isotope being used, the particles it emits, and its half-life; the optimal thickness, the grain size, and the speed of the photographic emulsion; and the optimal thickness of the tissue-section and the concentration of the radio-isotope within it.

The benefits of better resolution can be inferred from the limited investigations which have been made into deposition of radioactive isotopes in bone. Martland and Humphries[9] and Gettler and Norris[10] could show that Ra radium localised in bone rather than soft tissue. Pecher[11] and Treadwell et al.[12] showed that strontium tended to be more concentrated in areas of new-bone formation. Copp et al.[13] demonstrated that (unlike strontium) yttrium, cerium, and plutonium were deposited initially not as the bone-salts themselves but in the osteoid matrix. Bloom et al.,[14] on the other hand, claim that C^{14} is deposited primarily in areas of pre-existing bone. Now that the resolution can be improved from the estimated 15μ obtained by Hamilton's method to about 2·5μ by the method of Pelc,[15] there is hope that we shall be able to identify in individual cells deposits of isotopes with radiations of short paths such as α emitters and low-energy β emitters.

LINGUAL CANCER

CARCINOMA of the tongue is a comparatively rare disease, and few detailed studies of large series have been published. Jacobsson[16] has made a clinical study of 277 cases treated at Radiumhemmet, Stockholm, one of the most famous treatment centres in Europe, between 1931 and 1942, and in his monograph he discusses the therapeutic methods employed and the relation of lingual cancer to sideropenia (Plummer-Vinson syndrome) in women, to tobacco, alcohol, syphilis, trauma, and leucoplakia. He regards tobacco as definitely predisposing, though this is difficult to prove. There also seems to be a correlation between lingual cancer and syphilis, and leucoplakia is confirmed as precancerous. Treatment at Radiumhemmet has been by teleradium for the primary tumour, any remnant present after this being subjected to implanted radium needles or electrocoagulation. Prophylactic block dissections of the lymph-nodes have not been performed. If cervical metastases were present when the patient was first seen these were treated by teleradium, followed by operation if any remnant was detected. Every patient was carefully followed, and an operation was done on the untreated necks as soon as metastases were suspected.

The incidence of the disease was found to be 1–2 per 100,000 of population. The proportion of women was no less than 45%; this remarkable figure, to be parallelled nowhere else except in Finland, seems to be explained by the high incidence of sideropenia in Sweden. A five-year cure-rate of 28% was obtained over the whole series, and this is highly satisfactory in so refractory a disease.

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Reconstruction

THE HOSPITAL ADMINISTRATOR TODAY

FROM A CORRESPONDENT

ONE of the most notable developments in the hospital world of the last half century in Great Britain and America has been the evolution of the hospital administrator. Fifty years ago he was primarily a secretary, who emerged on committee days and retired to his room to write out the minutes with his quill pen. True, he discharged certain other duties such as ordering the provisions and paying the staff; but Miss Nightingale's works clearly show the subordinate position he occupied. "Administration," she wrote, "is intended to enforce economy, so far as is consistent with the provision of requirements necessary for the sick." This negative tradition has exacted a heavy toll, and alas still lingers on; but about the turn of the century the hospital administrator began to play a much more positive part, and just before the first world war the movement was in full swing. A textbook published in 1913 said:

"Standards of hospital administration have been practically revolutionised within the past five or ten years, and the standards of hospital managers have changed within the same time. The man or woman who was a competent hospital director a few years ago may be today so far behind the times that the whole institution is out of date . . . whereas in the old days members of the medical staff were constantly harassing the superintendent of the institution for new things, new apparatus, new methods, nowadays it is the other way about . . . the hospital superintendent under the new order of things is suggesting new methods, new apparatus and is giving new inspiration to the medical staff wholly within the realm of administration."

Since those days there have been great administrators in hospitals on both sides of the Atlantic, sometimes medical and sometimes lay. In this country the lay tradition has predominated in the voluntary hospitals of England and Wales, and the Minister of Health has adopted this model in legislating for the new service.

The increasing complexity of the work has called for a steadily rising level of ability and capacity, and during the last twenty or thirty years the house-governor (the common change of name is an indication of the changing conception of the duties) has become a relatively well-paid and responsible officer. Indeed, broadly speaking, the best-administered voluntary hospitals have been those with the best house-governors.

The house-governor (perhaps we should now say the secretary of the management committee) is not primarily a secretary in the ordinary business sense of the word, though he has to be an efficient secretary as a side-line or he will soon find himself in difficulties. He has so to arrange his morning, and the delegation of duties among his own staff, that only a relatively small part of his day is devoted to letters, and that he is free to discuss this and that with the matron, the catering officer, and the other departmental heads who want to see him. He has to find time to lunch with the medical staff most days of the week, for this is his principal opportunity to establish a happy relationship with them. This is his chance to let them know that their troubles will find a sympathetic ear, and that there is no need to make a fuss in committee about many little things that admit of a simple solution. He has to be prepared to spend a good many of his afternoons in committee or subcommittee of one kind or another. No one man can undertake more than a limited amount of committee work of this kind and do it as it should be done; and if he is not equal to the job, or takes on too much, he will find that business is cropping up in full committee which has not been adequately discussed and digested beforehand. (Ought he not to have spoken to the chairman about this, or warned the matron that so-and-so was going to be difficult about that?)

The hospital management committee is a new creation, radically different from both its parents, and administrators trained in the voluntary and local-authority traditions are everywhere feeling their way towards a new pattern. The management committee was conceived by the Ministry as a unit—a real management committee controlling the hospitals entrusted to it. The old pattern, as exemplified in the voluntary hospital, centred upon a lay committee and a lay administrative officer, interlocking with a medical staff committee, a nurses' training school, and subsidiary activities. The new creation cannot all at once achieve this simple pattern, and in many cases it has to deal with several medical staffs, several nurses' training schools, and a multiplicity of lesser activities, which still centre upon the individual hospitals within the group. Is it going to simplify itself so that before long there is a single medical committee, a single nurses' training school, a single catering organisation, and so on?

If now, as an unintentional result of the grouping of hospitals under management committees, the house-governor or secretary were to become so occupied with the secretarial affairs as to revert and become the slave of the minute-book, we should have taken a serious retrograde step. In some areas, by reason of the number of hospitals and committees and subcommittees involved, there seems to be a danger that something of this kind may happen. The danger is minimised, though not avoided, where the secretaryship of the management committee is combined with the house-governorship of one of the hospitals in the group—an arrangement which on other grounds is strongly to be commended. A hospital secretary cannot maintain the proper personal contacts if he is located in an office removed from the scene of activity, and any secretary who finds himself so placed, out of excessive regard to the need for "neutrality" between two hospitals, should forthwith remove himself and all his office into one or the other; for otherwise he will soon forfeit all hope of being or becoming a first-class hospital administrator. It seems to be one of the defects of the new set-up that management committees are too large, and at present deal with matters which should be delegated to their staff.

The duty of the principal executive officer is to attend, as secretary, as many committees—and as many only—as will enable him to keep his finger on the hospital pulse. For the rest, he must know intimately all the hospitals concerned and the principal people working in them.

He must be always accessible and ready to help to compose differences and to anticipate troubles before they develop. He must find time, too, for keeping in touch with the way in which other people are solving problems similar to his own, and never be so much busied with the routine of his office as to fall out of step with what is happening in the hospital world outside. If he has not got a capable assistant he must get one before disaster overtakes him.

He needs a clear desk and a stout heart. Dare we say it, he should not be over-conscientious in marking and digesting every paper that reaches him from official sources. He should realise that those who drafted them must often rely on him to interpret the spirit rather than the letter. Adapting a penetrating remark of the late Dr. Goldwater's to the conditions that now prevail in our nationalised hospital service we may say: "What the committee *like* is a secretary who will see that the H.M.C.'s and the R.H.B.'s are duly noted and enforced; what they *need* is an executive capable of initiating measures to fit the hospital's work to the needs of the community . . . and maintaining the health and spirits of the whole body of the workers in the hospital."

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Special Articles

HEALTH SERVICES IN FRANCE

DR. BRIDGMAN'S CHADWICK LECTURE

In a Chadwick lecture, delivered last week under the chairmanship of Lord AMULREE, the development and organisation of health services in France was discussed by Dr. R. F. BRIDGMAN, of the French ministry of public health.

This ministry, he said, had a difficult birth. Originally part of the ministry of home affairs, it passed into the control of the ministry of labour; and it gained full independence as lately as 1930. The ministry has two main divisions—public health and population. The public-health division is especially concerned with general hygiene, hospitals, social diseases, and organisation of the medical and paramedical professions; while the population division controls public assistance, and also deals with demography, immigration, and the integration of foreign workers into the community.

Each of the two divisions has representatives in the "departments"—departmental directors of health and of population, who act as technical advisers to the prefect. The directors of health are doctors but those of population are laymen. Their duties are largely complementary; for example, in hospital affairs the director of health supervises hygiene and equipment while the director of population is concerned with finance.

In the large field of health the minister is assisted by four further services: the Institute of Hygiene, as the research centre; the Central Service of Pharmacy, which controls the application of this profession's rules and classifies drugs; the Institute of Demographic Studies, attached to the population division; and finally the National School of Public Health, which affords post-graduate training to doctors seeking to enter the administration.

HOSPITAL ORGANISATION

Doctors in France number just over 30,000, most of whom are general practitioners; last September there were 2375 qualified specialists. Hardly any doctors are engaged full time in hospitals, except in mental institutions and in sanatoria.

Most hospitals are municipal; only three are directly controlled by the ministry, and very few are voluntary. Nursing-homes, belonging to surgeons or to commercial companies, are numerous. The municipal hospitals are run by an administrative committee always presided over by the mayor of the town, who is assisted by representatives of the municipality, the prefect, the medical staff, and the Social Security Board. The directors of health and of population may attend meetings but cannot vote. A lay director is responsible for personnel and administration. These municipal hospitals, though normally self-supporting, may receive ministry grants of up to 20% of the cost of exceptional expenditure on buildings or equipment. Paris, Lyons, and Marseilles, however, have a different system—the "Assistance Publique." In Paris this is a huge organisation with nearly 50,000 beds in general and special hospitals, sanatoria, preventoria, convalescent homes, and institutions for the aged. In every town institutions for the aged and for the chronic sick are run by the hospital authority; and most hospitals also have a section for the old.

Institutions for the tuberculous and for the insane are operated either privately or by the departments; there are hardly any municipal sanatoria or mental institutions. The public institutions are run by the departmental council—the "conseil général"—on whose advice the prefect appoints ancillary staff; directors and superintendents are appointed by the prefect. The department is principally responsible for building expenses; but 25% of the cost may be paid by the ministry. The dispensaries are run mainly by local authorities, though some have been set up by private societies and a certain number by Social Security.

SOCIAL SECURITY

France was comparatively late in evolving a comprehensive scheme of social security. In 1930 the first Social Insurance Act benefited two classes of people—industrial workers and peasants. Slowly the system expanded, and since 1945 it has been called Social Security. Altogether nearly 80% of the population is now insured. All employees are now covered against sickness and invalidity and for maternity and old-age benefits. From the start sickness insurance has included all workers' relatives for 6 months' illness. For chronic diseases, and tuberculosis in particular, benefits continue for three years. There are two sorts of benefit: (1) reimbursement of half the normal salary lost; and (2) a reimbursement of 80% of the doctor's fees. For some drugs 80% of the cost is paid, for others 60%; yet others are excluded altogether from the social-security lists.

Social Security is as independent of the ministry of labour as the municipal hospitals are of the ministry of health. Administrators of the central and regional funds are in a position to exert profound influence in the field of preventive and curative medicine and over medical practice. These administrators, who are elected by the insured, are not civil servants. In some areas Social Security has equipped dispensaries and health centres, while in Paris it is organising two special hospitals; in each region it owns several preventoria and rehabilitation centres. The power of Social Security to intervene in professional matters explains the difficulties which constantly arise between it and the medical profession. Further progress in medicine is possible only if Social Security continues to reimburse patients for the greater part of their expenses.

THE DOCTORS' VIEWS

For their part French doctors adhere to four principles: (1) freedom of choice; (2) freedom in prescribing; (3) professional secrecy; and (4) direct payment of fees without interference by any organisation. Economic difficulties, however, make it hard to preserve these principles. Fees are fixed in accordance with the amount of the benefits, and Social Security exerts control on professional activities and fights against abuses. The general practitioner's life is filled with papers and statistics demanded by Social Security.

For single-handed practitioners the price of equipment is very high, and to start in practice young doctors have to borrow money; so the profession has to consider team-work in health centres. They are unable to start centres themselves, and yet do not wish to practise in centres run by Social Security. For specialists the difficulties are even greater. Among students and young doctors there is a strong movement towards full-time practice in hospitals; but here too Social Security is the most important contributor, paying two-thirds of the general costs; it grants 80% of the cost of patients' stay, and 100% of the cost of major operations and of care of the chronic sick for 3 years.

FUTURE ORGANISATION

France has about 1400 hospitals with 190,000 beds. There are about 4 beds per 1000 population for the treatment of acute diseases; this number seems fairly adequate, but there are too many small hospitals and the large ones are not well equipped.

Reorganisation is to be based on a regional scheme, each region (with 2–3 million inhabitants) having a

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hospital centre, linked with a school of medicine, comprehending all specialist services. As well as the regional hospital centre there will be other hospital centres with general medical and surgical and some specialist services; each of these centres will serve 300,000–400,000 inhabitants. Both forms of hospital centre will serve as general hospitals for the immediate district. At the periphery will be simpler hospitals, each serving 50,000–75,000 people, with general medical and surgical, maternity, infectious-disease, and sometimes tuberculosis, departments; there will also be out-patient clinics for ear, nose, and throat, eye, gynæcological, and skin and venereal diseases.

Health centres will be of two types; (1) those with 10–20 maternity beds and cots and a small nursing unit for observation and emergencies; and (2) small centres with only dispensaries and technical facilities for medical team-work. Almost all centres of the first type will be beside a "hospice" for old people.

Unfortunately the hospital Act of 1941 does not enable the several types of hospital to be closely integrated. Municipal independence and individualism remain; plans submitted to the ministry are too large and are conceived without regard to coördination. A new measure is being prepared to promote a hierarchical organisation. By this, hospitals will still have their autonomous administrative committees, but coördination will be achieved through a departmental board; above this, a regional council will coördinate hospitals, sanatoria, psychiatric units, and health centres; and at the top the minister will be assisted by a national council. [This met for the first time last week.]

FURTHER EVOLUTION

There is one general practitioner for about 2000 of the population, and one specialist for about 7800. The number of doctors, which has doubled since the start of the century, is increasing rapidly. Before the late war the average number of first-year medical students was 1500; in 1947 there were 4500, and it is expected that by 1953 the number of doctors will have increased by 7000 in six years. Accordingly "it is quite impossible for a young doctor to find a new post.... The time seems favourable for a radical change in the conditions of practice and for full-time work in hospitals and health centres." Here Social Security is in a powerful position. Unfortunately its representatives sometimes misunderstand the true character of the medical profession and this opens the way to conflict. "In this light it is easy to understand why evolution seems so difficult in France."

The peculiarities of Social Security are both a strength and a weakness.

> "I believe it is good that Social Security has an independent budget and is considered as a voluntary institution. I think it is bad that representatives of Social Security are elected and are politicians rather than technicians. I consider also that having mixed social insurance and medical guarantee is a serious defect."

The minister, who is in full accord with the doctors, would be better placed than Social Security to discuss the future of the medical profession; but he has no power to intervene.

Reform of medicine is urgently needed, and this is a matter for government. There are at the moment two forms of hierarchy; one is academic, the universities granting various forms of postgraduate diploma; the other is a hospital hierarchy. Lately the qualifications required of specialists have been determined by law, and Social Security now reimburses patients under specialist treatment at a higher rate. "It would be efficient to unify these two parallel systems."

PUBLIC HEALTH MEDICAL OFFICERS

Salary Proposals

AT a meeting on Jan. 12 the council of the British Medical Association expressed its dismay at the continuing delay in settling the permanent remuneration of medical officers in the public-health service. The following resolutions were passed unanimously:

1. That the Ministry be informed of the serious unrest and dissatisfaction among members of the public-health services occasioned by the continued delay in the opening of negotiations on new scales and conditions of service.

2. That the Ministry be informed that if negotiations through approved Whitley machinery have not begun by Feb. 28, advertisements from local authorities will not be accepted by the *British Medical Journal* unless the salaries offered are in conformity with the association's own proposals for new scales.

3. That negotiations be conducted on a national basis covering England, Wales, and Scotland.

4. That the association's representatives on the public-health subcommittee of the medical functional council be: the chairman of council or his nominee, the chairman of the public-health committee, C. Metcalfe Brown, G. F. Buchan, Charles Hill, J. A. Ireland, R. H. H. Jolly, Jean M. Mackintosh, Wyndham Parker, J. Riddell, J. S. Stirling.

SUGGESTED SCALES

The public-health subcommittee of the Negotiating Committee has proposed the following scales, which include 20% betterment as in the Ministry's proposals relating to general practitioners' remuneration. This percentage has, however, not yet been accepted by the committee and is subject to further negotiations.

1. *Medical Officers in Departments.*—These are officers who, although without responsibility for the work of other medical officers, have had at the time of appointment at least three years' experience in the practice of their profession after qualifying. Salary: £960 per annum rising by annual increments of £60 to £1680.

2. *Senior Medical Officers.*—These are medical officers (not being medical officers of health) who are in charge of services or departments (for example, port-health, school-health, mental-health, maternity and child-welfare, or any other similar service or combination thereof), and who are engaged solely or mainly on such duties. Salary:

Population	*Minimum*	*Annual increments*	*Maximum*
	£	£	£
<300,000	1680	120	2160
<500,000	1800	,,	2280
<750,000	1920	,,	2400
750,000 +	2040	,,	2520

Where a medical officer in section 1 is in charge of a service(s) or department(s) but is not solely or mainly engaged on such duties, he should be remunerated on the scale of section 1 with an addition of £100 per annum. Such an arrangement would obtain in a local authority with a population so small as not to justify the appointment of a medical officer solely or mainly engaged on the duties of a senior medical officer.

3. *Deputy Medical Officers of Health.*—These are medical officers employed primarily as administrative deputy medical officers of health. Salary: the scale shall be not less than that appropriate for a senior medical officer in section 2 plus £100.

4. *Acting Deputy Medical Officers of Health.*—In areas where no deputy medical officer of health as defined in section 3 is necessary, a senior or departmental medical officer appointed to act as deputy in the absence of the medical officer of health, shall receive an addition to his scale salary of not less than £100 per annum.

5. *Medical Officers of Health.*—(*a*) Whole-time (all classes of local authority):

Population	*Minimum salary*	*Annual increments*	*Maximum salary*
	£	£	£
<100,000	1920	120	2400
<200,000	2160	,,	2640
<300,000	2400	,,	2880
<500,000	2640	,,	3120
<750,000	2880	,,	3360
750,000 +	3120	,,	3600

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(*b*) The salary of a practitioner appointed as a part-time medical officer of health shall be $\frac{x}{11}$ of the appropriate salary, according to population for a whole-time medical officer of health, plus one quarter of $\frac{x}{11}$ or one quarter of $\frac{11 - x}{11}$ whichever is the less, where x represents the number of half-days per week, or their equivalent, devoted to the appointment.

6. *Combined Appointments.*—(*a*) Where a doctor acts as medical officer of health to more than one authority he shall receive a salary-scale not less than £120 above the appropriate scale in section 5(*a*) indicated by the total population of the combined districts for which he is medical officer of health.

(*b*) Where a combined appointment is part-time paragraph (*b*) of section 5 shall apply.

(*c*) In Scotland, where a county medical officer of health is also school medical officer for the county and for one or more large burghs, the population of which is not included in the population of the administrative county, he shall receive a salary-scale not less than the appropriate salary-scale in section 5(*a*) above indicated by the total population of the administrative county and large burgh(s).

7. *Divisional or Area Medical Officers.*—These are medical officers appointed by local health authorities for divisional administration of the health services (including the school medical service). They fall into two classes:

(*a*) divisional medical officers acting also as county district medical officers of health. The salary-scale shall be that appropriate in section 5 according to population of the division or area, or population of the county district(s) for which he is acting as medical officer of health, whichever is the greater:

(*b*) divisional medical officers not also acting as county district medical officers of health. The salary scale shall be that appropriate in section 2, according to population of the division or area.

8. *Specialists.*—Where a whole-time medical officer in any of the above sections is employed partly by a regional hospital board and partly by a local authority, his total remuneration shall be the whole-time remuneration recognised by the regional hospital board for the type of work undertaken for them, or the salary-scale appropriate to his position in the local authority, whichever is the higher.

FURTHER PROPOSALS

Special Awards.—The subcommittee proposes that a proportion of medical officers of outstanding professional eminence in the public-health service should receive as a special award payment in excess of the remuneration provided for in the scales. Such awards should be made on the recommendation of a specially appointed committee mainly professional in character, including members of the medical profession, representatives of the universities, the Medical Research Council, the Ministry of Health, and the associations of local authorities. Such awards would be made in recognition of professional merit and scientific work done for the advancement of public health. They would be personal in character, and once made would continue to be received by the medical officer so long as he remained in the public-health service.

Other Conditions.—It is proposed that medical officers holding appointments in the County of London shall receive £120 per annum in addition to their scale salaries, and that those holding appointments outside the area of the county but within the Metropolitan police area shall receive an additional £90 per annum. Among the other conditions laid down are that the scales shall operate from July 5, 1948; that there shall be no differentiation on account of sex; that for teaching duties additional remuneration shall be payable; and that all grades shall be given at least 6 weeks' holiday a year, including public holidays. The report also names conditions to govern allowances during absence through illness.

Advisory Committee.—The subcommittee calls for the appointment of an advisory committee to consider:

1. Any case in which an authority proposes to employ an officer on conditions not in accordance with these scales and conditions.

2. Any difficulties in the application of the scales and conditions.

3. Recommendations by the committee which is to consider special awards.

The subcommittee observes, however, that all references to the advisory committee might go to the Whitley machinery, once this is set up.

HEALTH CENTRES

THE Central Health Services Council has appointed a committee to consider and make recommendations on the lines along which health centres should be developed under section 21 of the National Health Service Act. The members are:

F. MESSER, M.P. (chairman); F. J. BALLARD, G. O. BARBER, M.B., A. BEAUCHAMP, M.B., D. CAMERON, M.R.C.S., Sir ERNEST ROCK CARLING, F.R.C.S., Sir ALLEN DALEY, F.R.C.P., L. FINDLAY, M.D., Captain S. H. HAMPSON, Miss M. E. HOLLINGWORTH, S.R.N., R. H. HENRIKSEN, M.P.S., R. D. LAWRENCE, F.R.C.P., Prof. J. M. MACKINTOSH, F.R.C.P., Prof. R. H. PARRY, F.R.C.P., A. TALBOT ROGERS, M.B. (vice-chairman), Miss BLANCHE SHENTON, S.R.N., Mrs. DOROTHY THURTLE.

The secretary is Miss E. G. Long, of the Ministry of Health. The committee held its first meeting on Jan. 18.

COMPREHENSIVE CENTRE FOR LONDON

The first new centre to be approved by the Minister of Health under the National Health Service Act is to be built on the Woodberry Downs estate, Stoke Newington, at an estimated cost of £187,275, excluding equipment. Construction, starting next month, is due for completion in two years.

The centre is to serve an area with a growing population, which is likely to number eventually some 18,000; but it is expected that people from other districts will also attend. It will provide general-practitioner and dental services, antenatal and postnatal clinics, a child-welfare clinic, a school treatment centre, and other services, possibly including a foot clinic. Each of the principal departments has a separate entrance. There will be rooms for specialists.

The central entrance leads to a small waiting-hall with record office and inquiry counter, nurses' room, and lavatories. Corridors lead off to six suites of rooms for medical practitioners. Each suite has a waiting-room, consulting-room, examination room and dressing cubicle, and exit lobby. Also on the ground-floor is a small isolation ward with exit for easy removal of patients by ambulance.

A staircase leads to the first floor, where there is a bedroom, bathroom, and lavatory for the doctor on night duty, and a common-room with small service kitchen for general use by the medical staff. On the same floor are a small drug store; a clinical side-room; an eye room with dark-room, store, and orthoptic room opening from it; a duty-room; and a store-room. The centre of the first floor in this part of the building provides a waiting-hall with record office and inquiry counter. A corridor leads to two dental surgeries with recovery-room between and a dental workshop. A minor-operations room with dressings-room, sterilising-room, and recovery-room are also in this part of the building.

The school health unit has a waiting-hall, a room for dealing with minor ailments, a consulting-room, a nurse's room, and a record office—all on the ground-floor. Immediately above are two dental surgeries, with recovery-room and two dental workshops, and an eye-room with dark-room, store, and orthoptic room.

The child-welfare unit has a toddlers' room, milk-room, and store. A corridor leads to a lecture hall with platform and a demonstration kitchen attached. Off the hall is a suite comprising an undressing space, an interview-room for

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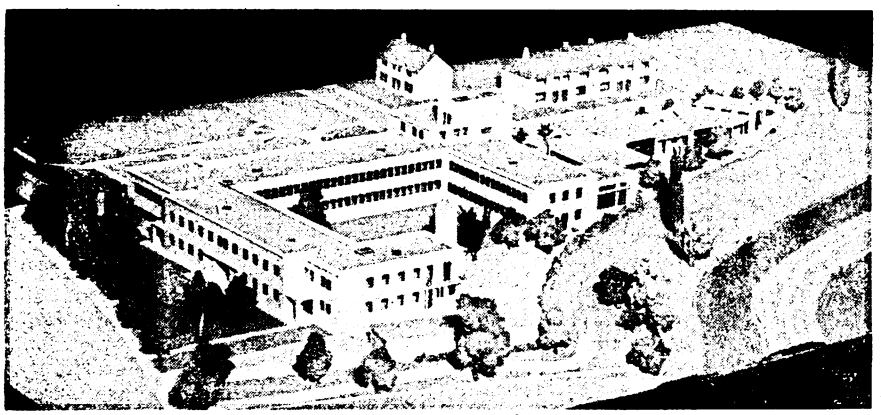

health visitors with test-feed room attached, a weighing-room, and waiting-space for patients.

The antenatal unit shares a waiting-hall with the child-welfare unit. Interviewing-rooms for health visitors and midwives, an advisory room with undressing cubicles and urine-testing accommodation, and a doctor's consulting-room are provided. On the first floor an ultraviolet-light room and an X-ray room will be available to all units.

The remedial-exercise and child-guidance unit consists of a play-room and rooms for a psychiatrist, a psychiatric social worker, and an educational psychologist. There is also an office and a room for orthopædic and remedial exercises, with an undressing-room attached.

To the east of the centre a day-nursery is to be built. There will be a lock-up garage for each doctor.

At a press conference last week, Mr. A. REGINALD STAMP, chairman of the health committee of the London County Council (which, as the local health authority, is responsible for centres in London), explained that the first aim was to provide one centre in each of the nine health-service units of the county; and the Minister had agreed to this in principle. It might be possible to provide some by modification and extension of existing centres, such as those at Finsbury and Bermondsey, which were not comprehensive; and already the council was on the way to acquiring sites for 40 new centres. The eventual aim was to have 162 centres—one for every 20,000 of the population, this number comprising two neighbourhood units each with 10,000. The Ministry had instructed the council to rent accommodation to doctors in the new centre at an "uneconomic rent."

Disabilities

22. MYASTHENIA GRAVIS

MY myasthenia started early in 1925, when I was 18. For several months it consisted of double-vision and fatigue. This did not worry me unduly, for I was an art-student at the time, and it seemed likely that these symptoms were the result of eye-strain and the long hours of standing at my easel. An ophthalmic surgeon told me that there was muscular incoördination of the eyes, and prescribed glasses with a prism.

Soon, however, more alarming symptoms began. The first occurred when I was ironing a dress and suddenly found that I could not hold up my head; it kept drooping forward. Then my knees started to give way under me at odd times, especially after running, and often on dismounting from my bicycle. My eyelids would droop uncontrollably when I was tired—far more than in ordinary sleepiness—and after painting for a while my arm would drop to my side. And so it was with all forms of muscular exertion; my movements, whatever they happened to be, would start to flag, and I would have to stop and rest. After a short while I would feel my strength returning and be able to carry on. This flagging of strength is difficult to describe. "Weakness" was not the impression it gave me. It was more like a cutting-off of my movements from my mind. I felt that my muscles were perfectly strong yet I could not make them respond to my will—just as in a nightmare one becomes rooted to the spot in an emergency.

By this time I was badly frightened, but I tried hard to swallow my fear and fight the symptoms, because I hated the thought of leaving the art-school. I was working for a diploma at the time, and loved my work. Being the only child of rather over-anxious parents, I revelled in the freedom of art-school life. And above all I was unofficially engaged to a medical student. I was very much in love, and we could often meet for a meal. Nevertheless, I had to give in and stay at home. My parents became alarmed, and I was sent to an eminent neurologist.

This was a horrible experience. He examined me thoroughly but could find no physical signs; and I, being at the best of times a nervous and imaginative creature, and by now scared out of my wits, made a very bad impression on him. He declared me to be suffering from hysteria, and asked me what was on my mind. When I answered, truthfully, that nothing was, except anxiety over my symptoms, he replied, "My dear child, I am not a perfect fool . . .," and showed me out.

At that time the disease was fluctuating in an extraordinary way. Soon after my twentieth birthday I was, at my worst, as bad as I have ever been subsequently; yet on some of my better days I was practically normal. I began to notice that the relapses always occurred about a week before my menstrual period was due, and that I improved again just before or after the period started. At my worst I could not turn over or sit up in bed without help, chew my food, or keep my eyes properly open or my mouth shut. Even speaking became difficult, for my tongue and vocal cords at these times were as useless as the rest of me. At this stage, however, these relapses were infrequent and always ceased surprisingly suddenly.

That was in 1926, and the next year was a nightmare. My trouble was still believed to be functional, and one "cure" after another was tried, including a course of psycho-analysis. I was in despair, for, deep down, I could never quite believe that my symptoms were purely hysterical. By the summer of 1927 the completely helpless phases came round almost every month, and at my best all I could do was to walk a hundred yards or so with a stick, leaning on somebody's arm. I was sometimes driven to a cinema, theatre, or concert—but inquiries had always to be made regarding the number of stairs on the way to my seat, and these expeditions were fraught with anxiety. I was helped with dressing and undressing, assisted or carried upstairs, and washed in a kneeling position in the bath.

My parents were wonderfully patient with me, but I was always haunted by the feeling that I was expected, sooner or later, to "pull myself together," and I knew that I couldn't. Yet for some reason I was bitterly ashamed of my condition. I was always trying to pretend

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to my friends that I was not ill, and making all sorts of excuses to explain my odd state of health.

Meanwhile my fiancé, who was still a medical student, had never ceased in his search for a true diagnosis of my trouble—for he, like myself, could not accept the theory of a neurosis. His efforts were at last rewarded when, in the autumn of 1927, he read about a case of myasthenia gravis. I saw the doctors in charge of that patient, and the diagnosis was confirmed in my case.

There was at that time no known treatment and therefore many things to try. For the next eight years I tried them all—gold injections, thyroid, suprarenal extract, lecithine, glycine. Ephedrine was the only one which seemed, occasionally, to cause slight improvement. I was twice admitted to hospital—the first time, in 1929, for experiment and investigation under a well-known neurologist, and again two or three years later for deep X-ray treatment of the thymus gland, which was said to have been successful in some cases, but unfortunately did nothing for me.

A resident nurse was engaged to look after me, and I spent most of my days in a wheel-chair. During those years my condition was, if anything, slightly worse. Being by nature rather restless, with a great love of independence, I bitterly resented the life I was now compelled to lead, and my frame of mind was not helped by the fact that before my illness I had taken a conscious pleasure in walking and moving well. I must have been a dreadful patient. The two things I dreaded most were heat-waves, which knocked me out badly, and catching cold. Colds were terrifying, because often I had not the strength to cough and the unrelieved tickle would send my wind-pipe into a violent spasm, causing me to choke (so I thought) nearly to death. But I was not always unhappy. Everyone was kind to me, and my fiancé insisted on remaining engaged to me, always maintaining that one day I would be well. I spent most of my time listening to my portable radio and reading, though this was an up-hill task, hampered as I was by double-vision and ptosis.

* * *

I had no real hope of recovery, but I eventually became resigned to my fate. Then, in February, 1935, came the day that I shall always remember. I was living alone with a nurse and housekeeper, my parents being abroad at the time. It was one of my better days, and I was lying on the sofa after tea, listening to the radio. My fiancé came in rather late, saying that he had something new for me to try. My first thought was, "Oh bother! Another injection, and another false hope." I submitted to the injection with complete indifference, and within a few minutes began to feel very strange. I seemed light-headed, and when I lifted my arms, exerting the effort to which I had become accustomed, they shot into the air. My upper eyelids were strongly retracted, and every movement I attempted was grotesquely magnified until I had learnt to make less effort. I had simply regained relatively normal strength—it was strange, wonderful, and at first very frightening.

Then I started trying all sorts of hitherto impossible movements. I found, for instance, that I could actually squat on my heels and stand up unaided! I walked across the room, feeling rather like a marionette on wires, and finally we danced twice round the carpet.

That was my first meeting with 'Prostigmin,' and we have never since been separated. My first injection was a small dose and wore off fairly soon. I could scarcely believe that I had not dreamed it, and felt certain that it was just a fluke and could never happen again. But of course it did, every time. Next day we went to the ballet. I shall never forget the thrill of marching into the foyer and up the stairs to the circle entirely under my steam. The other big thrill which I particularly remember was of being able to smile properly again, for a myasthenic smile is at best a dismal grimace.

At first I did not have prostigmin every day, because the day after an injection I seemed to be rather worse, and it was feared that the drug might do harm in the long run. This, however, proved to be wrong; for the tiredness was not due to any ill effects of the drug itself but to the exercise taken during its action. The obvious remedy was to be courageous and take it more often. This I did, and in a matter of weeks I was taking enough to be always under its influence. Within a few months prostigmin tablets became obtainable. I found that for a comparable effect the dose by mouth must be 30 times greater than by injection. As injections were more reliable and less likely to produce colic, I hit on the idea of dissolving tablets and filtering them to make injections. In those early days, when the drug was in short supply, this made it possible for me to have as much as I required. These experiments in chemistry were carried out in secret, with the aid of the housekeeper; neither the nurse nor my fiancé knew what I had done until I was sure that it worked.

Soon I became so independent that I could dispense with my nurse and say good-bye for ever to that hateful wheel-chair. In the summer of 1937 we were married. When the war came my husband was posted to an emergency hospital in the country. We took a small house nearby, labour was scarce, and I had to learn to cook. I managed fairly well, and was quite happy and confident indoors and in the garden, but could never go out by myself, for my movements were rather jerky and I still had not learnt to trust my endurance.

In the spring of 1940 I started taking guanidine as well as prostigmin. Within a few days it was obvious that this was the greatest advance in my treatment since the first dose of prostigmin. I gradually found myself able to run, go for short walks, and eventually do my own shopping, including queueing and carrying heavy baskets.

I was now managing so well that, in 1942, I applied for part-time work in a tank-factory, and to my delight was accepted. During my three years at a bench in the view-room I was often picked out by the foreman for a heavy job, on the grounds that I was "one of the tough ones"! No-one, in fact, guessed my secret throughout the time I was there.

One big set-back I brought on myself. Through fear of being caught unprepared by an air-raid alert, I had gradually increased my doses of guanidine. I developed a severe cystitis which defied diagnosis (in spite of three cystoscopies and numbers of guineapigs), until I agreed to cut down the guanidine, when cure followed very quickly. After this grave warning I have never taken more than 150 mg. two or three times a day.

After the war we returned to our London suburban home. I am still running the house with the aid of a charwoman on three mornings a week. I do all the shopping, which involves walking and bus journeys, and a lot of my spare time is spent in rediscovering London. I still make up my own injections from prostigmin tablets, simply because I am used to that particular strength—two 15 mg. tablets of prostigmin and four gr. $^1/_{100}$ tablets of atropine, dissolved in a tablespoonful (15 ml.) of water. I inject from 0·5 to 0·75 ml. of this mixture into the thigh or buttock about every two hours during the day and whenever I happen to wake in the night.

The very few people who know about my disability seem rather horrified at the idea of so many injections, but I find them no trouble at all, apart from occasional bruising or embarrassing specks of blood on my undies. I carry my outfit with me always—in my handbag—two of everything, contained in two flat spectacle-cases. All I do to prevent sepsis is a weekly boiling of

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syringes, and a daily hot bath and change of underwear. Years ago I religiously rubbed my skin with spirit or ether before each injection, but as nothing untoward happened on the few occasions when I had no spirit with me I dropped the habit, and I have never had cause to regret it. The injection can be done in a few seconds, with so little trouble that I have sometimes, when distracted, been unable to remember, five minutes later, whether I had had it or not.

An overdose of prostigmin (through carelessness) can be mildly unpleasant, causing epigastric ache, sweating, and slightly blurred vision; but gr. $^1/_{100}$ of atropine taken by mouth soon puts it right. I always carry a spare tube.

Of course, in a mild way I still have my ups and downs. There are days, particularly before my periods, when I would prefer not to walk more than a quarter of a mile at a stretch; and on which I have trouble with holding my arms up to brush my hair or scrub my back. On these days, too, I may see double, and have to cover one eye while reading. Some of my old activities I avoid altogether, knowing that I could not sustain them. I never play tennis, ride, or play the piano seriously.

Otherwise I lead a full and happy life. My general health, digestion, and appetite have always been good, and I feel (and I'm told look) considerably younger than my 42 years. During my cystitis I was anæsthetised three times without giving my doctors any anxiety.

One day I shall take up painting again, but at present the joy of the daily renewal of freedom of movement makes me eager to be out and about during my leisure. Every morning, after several hours without prostigmin, I awake to a reminder of what life used to be. Then, a prick—my strength flows back, and I am myself once more.

Public Health

Influenza

INFLUENZA deaths in England and Wales during the week ended Jan. 15 numbered 40, compared with 47 in the previous week. There is as yet no indication that influenza has invaded this country in epidemic form.

According to W.H.O., almost the whole of France is now involved, with about 20% of the population affected. It is understood that strains from France and Holland seem to be of the A type. Inquiries up to date suggest a closer resemblance to the strains observed in 1947 than to the classical P.R.8.

Statistics for 1948

Three new health records were set up in England and Wales in 1948. They were for the number of babies dying under the age of one year, stillbirths, and the general death-rate.

The Registrar-General [1] reports that the total number of deaths registered in England and Wales during 1948 was 470,282, the lowest number for 18 years despite an increase of some $3^1/_2$ million in the population at risk. This represents a record low death-rate of 10·8 per 1000 total population—an improvement of 1·2 over that for 1947.

There were 26,635 deaths of children under one year of age, giving a rate of 34 per 1000 related live births. This is the first time the annual rate has fallen below 40, the previous lowest being 41 in the previous year.

Stillbirths numbered only 18,415, giving a rate of 23·1 per 1000 live and still births. The previous lowest rate was 24·1 in 1947.

The number of live births was 777,648—a reduction of 109,172 from the peak of 886,820 in 1947, but still substantially above pre-war levels.

1. Registrar-General's Weekly Return for the Week ended Jan. 15. H.M. Stationery Office. Pp. 20. 6*d*.

In England Now

A Running Commentary by Peripatetic Correspondents

IN my view the only way to run a health service properly is to make it a comprehensive health service. I would attach each G.P. to a particular hospital. He would "feed" that hospital and be served by it. He would get to know the residents and the visiting staff and would in fact become one of the team, and the team would help individual members of the team. It would be a good thing to bring the G.P.'s into closer contact with the hospitals and to bring the junior residents into closer contact with the problems of general practice. At the moment there is a wall between the general practitioner and the hospital services. It is not a very high or very thick wall, but one cannot see over it. One can however hear the wail coming from each side of the wall about what those on the other side are doing or not doing. Each of course says that the other either spends all his life drinking cups of tea or failing to examine a patient and signing certificates ad lib. Both statements are libellous and untrue. Remove the wall and much of the backbiting and misunderstanding will cease.

* * *

CUCKOO SONG: 1949 VERSION

Patients keep icumen in—
I shall go cuccu
If once more I hear that door
Swinging fro and to—
Quite cuccu.

More glum faces come,
Coughing with the 'flu.
Gaffer wheezeth, infant sneezeth,
Almost I'm cuccu.

Almost cuccu? Why no, *quite* cuccu
What am I to do
Being cuccu? Why *act* cuccu.
Be cuccu, join cuccu queue.

* * *

We are a funny inconsistent lot, we doctors. We insist on eliciting nearly all our patients' physical signs ourselves, because we have been trained (we think) in accurate observation, but in hospitals we leave the observation of the most universal and fundamental physical signs to the nursing staff, who have not been trained to make accurate observations, except by unreliable rule-of-thumb methods.

Of course, deliberate deception is rare—though at my old hospital there was (and still is) one old tartar of a sister who occasionally made up the temperature charts in advance to suit her views on prognosis before she went off for the weekend, and any patient who displeased her had a normal T.P.R. on his chart until the physician was convinced and discharged him. Accidental or ignorant deception, however, is common. The error of temperature-taking in children has recently been discussed by Professor Moncrieff in the *B.M.J.* But what about errors in adults? My experiences as a patient are limited, but I was recently in a private ward for 3 weeks for investigation (among other things) of a pyrexia of uncertain origin. My temperature was taken "four-hourly" (or more precisely five times a day, for the intervals varied greatly) with a thermometer which was kept in a tube of pink fluid in my room. I had easy access to my temperature chart and so could compare my real with my recorded temperature. Occasionally, the two coincided. Some nurses were very careful—one went into a trance for 2 minutes while the thermometer was in my mouth and another read the newspapers on my bed—but one (a night nurse and therefore always in a hurry) never left the thermometer in my mouth for more than 20 seconds and on one occasion charted my temperature as 97·4° when it was actually 100·2°.

The pulse-rate is so labile that accuracy is difficult. A pretty nurse may push a susceptible man's pulse up to abnormal levels very quickly and it is seldom that a

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nurse will count the pulse for more than 15 seconds. But it is on the question of respiratory rate that the element of raw farce first enters. The respiratory rate is irrelevant to all but a few conditions—indeed on many charts it is not plotted. The nurses know this and adopt a policy of recording 20/min. (or 24/min.; custom varies from ward to ward) unless the patient has obvious dyspnœa. When I was admitted I held my breath for the whole of the first visit for T.P.R. by the nurse. On the next I did a tachypnœa act (at about 40 R.P.M.). On both occasions my respirations were recorded as 20. Respiratory rates should only be recorded on demand, like other special investigations, when there is a particular reason to record them and when the physician will take note of the result. In my own ward we make a special study of respiratory rates, and every nurse coming on the ward is given special instruction on counting them. If an unexpected value is reported it is carefully checked by Sister, who takes a personal responsibility for the accuracy of all the records. Even so, we are now working on an automatic respiratory rate recorder.

What can be done about it all? I suggest, first, that all nurses should have proper instruction in the making of observations and their inherent errors. This should be achieved by giving them experiments to do designed to show the variation in recorded temperature with site and duration of observation, and to show the variation of pulse and respiration with emotion and exercise. All this instruction might supplant some of the time spent on teaching nurses obscure differential diagnoses. Secondly, we should develop better methods of automatic recording. I must see the gadgeteer physiologists about this. If A. V. Hill can record a rise of temperature of a millidegree in a frog's muscle on contraction he ought to be able to improve on the clinical thermometer. Pulse-rates could easily be recorded electrically on sister's desk from each bed. As I said before, we soon hope to have an automatic respiratory recorder for the patients who require it. Then the nurses might have more time for nursing.

* * *

The Atomic Physician has been at it again. The inspiration came to him in a flash (or possibly splash) when he dropped a winchester of radioactive urine on the floor and wondered, as he mopped it up, what would happen to the mice. His astute research mind at once grasped the possible applications of this random thought, and he set to work to perfect a radioactive cheese. This was not so straightforward as might have been expected. The radioactive material used had to have a hard gamma-ray emission for high penetration and a relatively short half-life to avoid contamination of the buildings. These problems, however, have now been solved and arrangements have been made for the distribution of a suitable cheese base through Messrs. Squeak and Nibble, Ltd. When required the radioactive material is obtained from the Atomic Energy Research Establishment at Harwell and dissolved in the base. At night the radioactive cheese is placed at vantage points in the infested rooms. Then next morning, all uneaten portions having been removed to reduce the background count, a search is made with a portable Geiger-counter for the radioactive mouse, which will show as a sudden increase above the background count. Having located the mouse you then bring up a loudspeaker connected to a microphone and tell the mouse that he is surrounded but if he surrenders he will be treated as a prisoner-of-war. If he emerges you can wring his neck with little fear of retribution (war-crimes tribunals being now out of fashion). More probably the mouse will suspect your motives and stay put. You are then left with three alternatives. You can: (1) pull up the floorboards, when the mouse will probably disappear through a secret passage; (2) hope that the wretch will die of agranulocytosis as a result of irradiation; or (3) buy a more orthodox mouse-trap from Woolworth's.

* * *

A Gynæchiatric Problem: "My Nannie is neurotic and I think the cause of her trouble is an introverted uterus."

Letters to the Editor

SENIORS AND JUNIORS

SIR,—Now that the State is paying for the services of the consultants at the hospitals it will be its duty to see that the services for which it pays are given in the best possible manner, and that no ancient or long-established traditions prevent this.

The relationship of senior and junior honorary staff, and the relative extent of their work in the hospital, has varied from place to place. In some hospitals juniors see outpatients only and have no beds; in others they see all the outpatients and have a few beds; and in others both the seniors and juniors see outpatients and the beds are divided in varying proportions among them. The new service more or less abolishes—or certainly makes less distinct—the difference between senior and junior, and many hospitals have themselves anticipated this by abolishing the title "assistant." Now, if the Spens report is accepted, consultants will be graded only by age or their good fortune in securing distinction awards. Whatever their income, they will be paid on the basis of doing the same jobs as their colleagues in the same department.

There is much to be said, therefore, for an even distribution of beds among the members of each department. At present a junior physician doing as many outpatient sessions as his senior may find himself unable to give his patients a comparable service because he has fewer beds at his disposal. Look at this from the other point of view. It means that a doctor sending to the outpatient department a patient ultimately needing hospital admission is not giving him as good a chance if he sends him to the junior as if he sends him to the senior. Obviously the State cannot pay for such an uneven service. Any patient sent to hospital for consultation should have the same chance of being investigated or treated, whether he is seen on Monday or Tuesday, by Dr. X or by Dr. Y. The State cannot supply two kinds of service at one hospital. Patients must not have different mathematical chances of being treated. This can be avoided only by abolishing the title "assistant," and by dividing the beds in any department equally among its members.

Emergencies provide an important part of clinical work and the question of their admission should be dealt with similarly. Instead of all being admitted under the senior member as is the practice in many hospitals, they should be admitted in rotation under each physician or surgeon. Only by such revision of our present practices can we hope to give the public a fair service and to maintain a high professional standard among consultant staffs.

SURGEON.

SKIN TUBERCULOSIS TREATED WITH PARA-AMINOSALICYLIC ACID

SIR,—In 1944 Lehmann [1] showed that *p*-aminosalicylic acid (P.A.S.) had a strong bacteriostatic action on the tubercle bacillus. This was confirmed by Youmans,[2] and Sievers [3] showed that the action was specific to the tubercle bacillus. The new remedy was found to cure experimental tuberculosis in guineapigs [4] and mice.[2 5] In clinical trials encouraging results have been obtained in pulmonary tuberculosis, fistulas, abscesses, and empyema.[1 6] At the Scandinavian tuberculosis congress last July G. Vallentin and his colleagues presented the results of treatment with P.A.S. in 378 cases of pulmonary tuberculosis (not yet published). Carstensen [7] has described 22 cases of intestinal tuberculosis treated with

1. Lehmann, J. *Lancet*, 1946, i, 15.
2. Youmans, G. P., Raleigh, G. W., Youmans, A. S. *J. Bact.* 1947, **54**, 409.
3. Sievers, O. *Svenska Läkartidn.* 1946, **43**, 2041; *Nord. Med.* 1947, **33**, 145.
4. Lehmann, J. *Svenska Läkartidn.* 1946, **43**, 2029; *Nord. Med.* 1947, **33**, 140; *Rev. gen. Sci.* 1947, **54**, 222. Feldman, W. H., Karlson, A. G., Hinshaw, H. C. *Proc. Mayo Clin.* 1947, **22**, 473.
5. Moeschlin, S., Jaccard, G., Bosshard, M. *Experientia*, 1948, **4**, 158. McClosky, W. T., Smith, M. I., Frias, J. E. G. *Fed. Proc.* 1948, **7**, 244.
6. Vallentin, G. *Svenska Läkartidn.* 1946, **43**, 2047; *Nord. Med.* 1947, **33**, 147. Dempsey, T. G., Logg, M. H. *Lancet*, 1947, ii, 871. Erdei, A. *Ibid*, 1948, i, 791.
7. Carstensen, B. *Svenska Läkartidn.* 1948, **45**, 729.

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P.A.S., usually with striking results. I have myself treated 80 cases of pulmonary tuberculosis with P.A.S. and have obtained good results, especially with exudative lesions.

As supplies are small, P.A.S. has seldom been used in the treatment of tuberculosis of less severe localisation. I wish therefore to report success in a chronic case of skin tuberculosis.

A man, aged 30, in whom bronchial tuberculosis and a tuberculous right calcaneus had been diagnosed in 1928, developed in 1933 bilateral lymphomata on the neck and extensive tuberculosis of skin on the lateral side of the right foot, probably originating from a fistula from the tuberculous calcaneus. The skin tuberculosis began to heal in hospital in 1934 but remained unhealed for the next fourteen years. During this time the lesion has persisted, with periods of exacerbation, ulceration, and exudation. When at its best the surface has been dry but without epithelisation.

In October, 1947, bilateral extensive pulmonary lesions with cavities were diagnosed. The patient was then admitted to the Central Sanatorium in Arvika. He was febrile, and his general condition was poor. The skin lesion covered an area of the size of a hand round the right malleolus. The surface was ulcerating and covered partly by exudate and crusts and partly by hyperkeratotic areas. Microscopy showed chronic inflammation of the corium and typical tubercles with giant-cells of the Langhans type. A pathologist reported the specimen as chronic tuberculosis of skin similar to lupus vulgaris.

In December, 1947, the patient was treated locally with Finsen light and mild keratolytic ointments. This treatment was continued to the end of February, 1948, without any notable improvement. Local treatment with P.A.S. was instituted on Feb. 25. The affected area was covered with gauze wetted with a neutral 10% solution of P.A.S., which was changed four or five times a day. The effect was dramatic. Already after a week the periphery of the lesion showed signs of healing, and after two weeks a zone 1·5 cm. wide round the ulcerating centre of the lesion had healed, becoming epithelised (see figure). After continued local treatment the lesion healed completely by March 29, and the treatment was discontinued. A few weeks later, signs of ulceration were seen in the centre of the lesion, and treatment with an ointment containing 20% P.A.S. was instituted, but without effect. After the application of a 10% solution of P.A.S. the lesion healed again rapidly, with epithelisation, and has remained for seven months unchanged.

The general condition of the patient did not improve during his stay in hospital. Being continuously febrile he rested in bed during his stay. No change was observed in his bilateral pulmonary lesions in spite of temporary treatment with P.A.S. by mouth and injections of streptomycin, which was administered after the healing of the skin lesion. It can therefore be concluded that the healing of the skin lesion was not caused by improvement in the patient's general condition due to ordinary sanatorium régime but must be ascribed to the local treatment with P.A.S.

Above.—Tuberculous lesion of skin 16 days after start of treatment with P.A.S. Dotted line indicates area affected before treatment. Below.—Same lesion after 34 days' treatment with P.A.S.

Arvika, Sweden. ROLF LEMMING.

PENILE CARCINOMA AND CIRCUMCISION

SIR,—In reply to Sir Ernest Kennaway's remarks (Jan. 1) on my letter of Dec. 18, I should like to say that my summary of his theory, far from being "nonsensical," gave clearly the essential feature—namely, that circumcision averts the subsequent development of penile cancer, but only if performed soon after birth.

As to numerical data, it is well known that Jewish women suffer from cervical cancer only very rarely. Ackerman and del Regato [1] write: "Jewish women, who are not immune from other forms of cancer, present a very low incidence of carcinoma of the cervix."

There is a contradiction in Sir Ernest Kennaway's [2] paper. He suggests that the absence of penile cancer in Jewish men is due to very early circumcision, and that in Moslems circumcision performed at puberty is not able to prevent this cancer. Yet he reproduces a table by Nath and Grewal [3] showing that the ratio of penile cancer to all cancers is in Hindus 1 : 3·9 and in Moslems 1 : 34·3. Thus circumcision *at puberty* might (if it *is* a determining factor) exert a considerable protective influence in Moslems.

All observations in cancer research seem to suggest that generally the most important factor in cancer-susceptibility is the very great difference in the susceptibility of cells in different species, classes, races, strains, and individuals.

London, N.W.3. HANS BAB.

INDEPENDENCE IN RESEARCH

SIR,—I have followed with interest the correspondence on this subject. The case for independence, particularly in fundamental research, is strong, the essential point being that the goal of science differs from that both of politics and of religion. Moreover, science has a different concept of "true" knowledge from either of the other two institutions. The conflict of science with religion and politics, from ancient Greece to the present time, has been due mainly to these two factors.

Science has been a very transient feature in human history. It was eliminated from the classical world by its two opponents because of its different goal. Greek science, like its modern counterpart, was concerned with the study of the material universe; it was not interested in man and his problems, either personal or social. This indifference earned for science the reproaches of most of the Greek philosophers from Socrates and Plato onwards, Aristotle excepted. Even Epicurus, who accepted the atomic theory, regarded science as the pursuit of "needless knowledge." Man refused to be ignored; the later Greek world insisted on the absolute supremacy of the inner life, and exhibited complete contempt for the material universe. Science therefore became pointless; the object of its study had been renounced. Science and its intellectual detachment were swamped, in Gilbert Murray's [4] phrase, by the "cry of the heart for salvation." This contempt of the material world passed over into Christianity, where it became even stronger; so the focus of man's attention became the other world, the world of the eternal spirit. With the eradication of science, rational medicine disappeared, because, as Singer [5] observes, "in the race for salvation, who will pause to consider this miserable tenement of clay?" Until very recently modern science, like its classical counterpart, has been equally indifferent to man; and its value has been questioned already.

1. Ackerman, L. V., del Regato, J. A. Cancer: Diagnosis, Treatment, and Prognosis. London, 1947.
2. *Brit. J. Cancer*, 1947, **1**, 335.
3. Nath, V., Grewal, K. S. *Indian J. med. Res.* 1935, **23**, 149.
4. Murray, G. Five Stages of Greek Religion. London, reissue 1943.
5. Singer, C. Short History of Medicine. Oxford, 1928.

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Science has never claimed to know everything. Religion on the other hand, has made that claim; and extensive claims have been made for politics on various occasions. For centuries Western Christendom was based on the *Summa Theologiæ*,[6] the work of Albertus Magnus and St. Thomas Aquinas. Two sources of knowledge were admitted—Christian faith through the Holy Scriptures, and human reason through Aristotle. Both these sources *had to agree* as each came from God. It claimed to explain the whole of existence and to comprise the whole of knowledge. Moreover, if events called for a reinterpretation of a particular point, the right to make this innovation was strictly confined to the *central authority*, which claimed the monopoly of having contact with fundamental sources. In other words, as Polyani [7] points out, the central authority of the Church demanded not only devotion to an orthodox system of beliefs but also the subordination of everyone's judgment to the discretionary decision of an official centre. Political systems, similarly, tend strongly to develop this centralised authoritarian pattern.

The history of science since the Renaissance has been largely the story of the rejection of this claim of the central authority to be the sole channel of access to fundamental sources of true knowledge. Moreover, the central authority has asserted that the method by which it reached this true knowledge was by revelation. Science, however, has demanded the most stringent tests before admitting the validity of such knowledge, and maintains that even so it is only a matter of probability. Politics, like religion, tends to claim that its knowledge is certain and irrefutably true. Yet, as Bertrand Russell [8] has said, "all definite knowledge belongs to science."

It is to be hoped that in the future this conflict will be resolved by a "deeper religion and a subtler science," [9] and it might be added, wiser politics. The present authoritarian trend, with its urgent utilitarianism, is more likely to destroy than to foster the source from which the solution of man's problems might come. Politics, in my opinion, are not yet fitted to control science.

Manchester. F. S. A. DORAN.

SIR,—It seems that I must agree to disagree with Sir Ernest Graham-Little (Jan. 15) on the question of the relationship of science to politics. I can only restate my opinion that if scientists do not consciously interest themselves in current politics they are in danger of becoming—if they have not already become—the unwitting tools of groups of individuals who are not at all interested in the progress of human society.

In judging Russian science we should apply to it those criteria we apply to all growing and developing things. We must ask ourselves the questions "What was it?" "What is it?" "What will it become?" In other words, we must not take Soviet science out of its space-time context. Soviet science is relatively young, and it is irrational to expect it to produce discoveries comparable with the development of vaccine therapy and penicillin. And I cannot accept Graham-Little's implication that spectacular discoveries necessarily mean that all is well in the world of scientific research. German scientists have given us much that is progressive, but they also gave us the flying and rocket bombs.

Graham-Little is right when he says that the "Lysenko incident" has evoked an extraordinary measure of attention all over the scientific world. It has rekindled an international scientific controversy, which will no doubt rage for many months to come. This is a good thing, for we shall all learn from it.

It appears that Graham-Little has easier access to Stalin's pronouncements than I have. I do not know what Stalin has said about Lysenko, but I do know that he once said that "science is called science just because it does not recognise fetishes, just because it does not fear to raise its hand against the obsolete and antiquated, and because it lends an attentive ear to the voice of experience, of practice."

Huby, near Leeds. P. J. WADDINGTON.

6. Dampier, W. Shorter History of Science. Cambridge, 1944.
7. Polyani, M. Science, Faith, and Society. Oxford, 1946.
8. Russell, B. History of Western Philosophy. London, 1946.
9. Whitehead, A. N. Science and the Modern World. Cambridge, 1946.

GENERAL PRACTICE

SIR,—After six months of the National Health Service it is obvious that the capitation fee is inadequate, and that the approach to the doctor is too facile. Our more human patients approach us rather shamefacedly, in that they cannot show gratitude in a concrete form. Our less pleasant patients demand our services as by statutory right, for minutiæ.

I suggest that the "no payment under any circumstances" clause be dropped, and that a nominal fee of one shilling be paid by anyone consulting his doctor, whether for blebs, blains, or childbirth, corsets or vacuum flasks.

Such a course will be welcomed by the great majority of our patients. Free treatment to the layman was ever bad treatment. It will relieve our waiting-rooms of those who demand a prescription for a self-diagnosed, self-treated, non-existent, complaint because it's cheaper than paying for a "cough cure" at the chemist's; and of those who pop in for a "thorough overhaul" because they missed a train and have an hour to waste.

High Wycombe, Bucks. G. E. CHURCH.

MORBIDITY AND FEEDING IN INFANCY

SIR,—I am grateful to Dr. Naish for her article (*Lancet*, Jan. 22) and letter (*Brit. med. J.* Jan. 22), extolling the advantages of breast-feeding. I would assure her that I hold no brief for bottle-feeding as a first-line assault on the baby. On the contrary, tradition, which is a powerful force, inclines me strongly to the natural method; and all babies in my practice, with rare and rebuked exceptions, are put to the breast. But one is always influenced by personal experience, and when one's first and second children have nearly starved for a fortnight or more before thriving on a bottle, one seeks some justification for the happiness obtained by starting the third and fourth on the bottle at the onset.

A recent correspondent elsewhere puts this poser, based on a 10% mortality in these infants from congenital pyloric stenosis: "If I were told that my next child was going to suffer from this unpleasant fate, would I still insist on bottle-feeding it in view of the added risk?" Without knowing whether the elder children would have actually died of starvation—the first lost over 3 lb. in the process—it is hard to say. But are these statistics sound? All the worst cases of pyloric stenosis I get to operate on have been tried out on all sorts of things in bottles as a desperate alternative to surgery; those still breast-fed are usually far better operative risks. Ought we really to rely on this bottle-feeding classification?

Another series of helpful statistics comes from the incidence of visits required in, say, the first year of life, which is admittedly far higher in the bottle class. I put this to my wife. She replied that maternal anxiety seemed to produce most of these visits, and that perhaps a laudable and cow-like placidity might be the reward of natural nursing for mother and child.

One last point. Ought breast-feeding to continue when the mother has heavy domestic work with other children and her periods have recommenced?

Deal. JAMES S. HALL.

NO ROOM AT THE HOSPITAL

SIR,—Dr. Wade in his letter last week (p. 164) says: "In some hospitals porters seem to deal with admissions and refuse patients without any reference to their medical staff." This innocent sentence may well be passed over as of little significance, so perhaps the following example may be of interest.

A doctor rang this service one evening asking for the immediate admission of a 7-month-old baby with acute bronchopneumonia, requiring oxygen, at the earliest possible moment. We rang up hospital A, which was near the patient, and were informed by the porter that he was not taking any more cases; we therefore had to try elsewhere and a bed was obtained for the baby at hospital B, further from its home. Owing to the urgency of the case an accident ambulance was called and the attendant, on seeing the baby, realised that there was no time to be lost; so, disregarding our orders—in my opinion rightly—he took the patient to hospital A and asked the porter to take the child in but was again refused.

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The ambulance therefore had to carry on to hospital B, where the dead child was delivered to the mortuary.

Is it conceivable that any responsible doctor would have refused to admit this baby on either occasion?

Emergency Bed Service, London, E.C.2. R. E. PEERS Secretary.

REGIONAL REPRESENTATION ON THE JOINT TUBERCULOSIS COUNCIL

SIR,—Dr. Gray's protest (Jan. 1) against the decision of the Joint Tuberculosis Council in not allowing the Liverpool Region Tuberculosis Society representation on the council, will, I am sure, have the sympathy of many of the doctors engaged in the tuberculosis service, even although the decision would appear to be constitutionally correct.

Dr. Gray's letter is an expression of the fairly widespread feeling of unrest and dissatisfaction amongst those engaged in this branch of medicine, arising no doubt from present trends which do not allow for direct representation of tuberculosis workers on the regional hospital boards and committees which are at present framing medical policy in the various regions throughout the country. The constitution of these bodies makes one wonder if the tuberculosis problem is now considered to be so simple that the planning of its control and treatment can be safely left to laymen and administrators.

Strathpeffer, Ross-shire. J. LANDESS HORNE.

STREPTOMYCIN IN HUMAN PLAGUE

SIR,—In an annotation on Jan. 15 you kindly gave space to a plea I had made, at a meeting of the section of epidemiology of the Royal Society of Medicine, for accuracy and precision in the presentation of statistics, for conclusions in accordance with them, and for tables rather than graphs. It is a pity that these standards were not applied to the article by Karamchandani and Rao published in the same issue and purporting to compare streptomycin with other treatments of human plague. Streptomycin may be of the utmost value but pseudo-statistical "evidence" like this must damage rather than further its case.

To take a side-issue first: the authors report that among 120 inoculated patients the case-mortality was 27·5%, and among 86 uninoculated 32·5%. Dividing up the inoculated they state that the case-mortality was "composed of 18% among those who had been inoculated 1–7 days, 4·5% among those inoculated 7–14 days, and 5% among those inoculated from 14 days to 4 months before the onset of plague." It is a trifle difficult to see how rates of 18%, 4½%, and 5% in subgroups can produce a rate of 27½% in their total, and no basic data are given to inform the reader. Reflection suggests that since 18, 4½, and 5 *add up* to 27½, the authors have not calculated the fatality-rates of the three subgroups at all (by dividing deaths in each by the appropriate cases) but have divided the deaths in each group by the 120 *total* cases irrespective of the state of inoculation. The resulting figures have no meaning whatever and certainly do not show "that immunity develops a week or so after inoculation."

Turning to the main issue, and neglecting half a dozen cases treated with sulphathiazole and penicillin, the authors show that of 153 patients treated with anti-plague serum, sulphathiazole, and 'Soluthiazole,' 28% died; of 32 treated with anti-plague serum and sulphadiazine 22% died; of 15 treated with streptomycin 20% died. No attempt is made to show that these groups were in any respects comparable with one another, but accepting them at their face value the upshot is clearly not very different. The authors, however, add that the last group was certainly not equivalent, that "streptomycin was given only to patients admitted apparently moribund or to patients who had become apparently moribund after admission, not having responded to sulphadiazine." This, in fact, is the whole substance of their case—not that the groups were comparable but that of 15 moribund cases treated with streptomycin 12 recovered. Well documented that would clearly be impressive evidence. Cluttered up with these uncontrolled and ill-described comparisons it merely loses much of its force. It also seems more than a little misleading to refer to the "brilliant success of streptomycin therapy, under which no patient died who was not already moribund when the treatment was started." According to all the previous statements in the paper no patient not already moribund has ever been given the opportunity of showing what he can do.

Department of Medical Statistics, London School of Hygiene and Tropical Medicine. A. BRADFORD HILL.

SIR,—I should like to make the following observations on the statement by Dr. Karamchandani and Dr. Rao, in their article of Jan. 15 that "inoculation did not give protection."

1. Sizes of inoculated and uninoculated populations exposed to the risk of plague are not known; therefore what proportion of the inoculated and uninoculated population at risk is represented by the 120 inoculated patients and the 86 uninoculated who were admitted with plague is not known.

2. The difference between the proportions of "moribund" cases on admission in the two groups is statistically significant:

	Inoculated % *of all cases*	*Uninoculated* % *of all cases*
Moribund	9·1 ..	18·6
Deaths	33 ..	57

3. From fig. 2 it appears that all cases treated with streptomycin were uninoculated. But for this treatment, mortality in this group might have resembled that in similar cases among the inoculated. The addition of these 12 cases would have given a mortality of about 49% (instead of 32·5%), compared with 27·5% in the inoculated group.

4. If, as stated, immunity develops a week or so after inoculation, then of the 120 cases the 22 (18%) inoculated less than a week previously may, I think, be regarded as uninoculated. This gives the following result:

	98 inoculated	*108 uninoculated*
Mortality	11·2% ..	46·3%
Mortality, without streptomycin	11·2% ..	57·4%

5. Figures regarding persons who were attacked (and either died or recovered) in the district but did not come to the hospital are not given. Intervals between inoculation and attack in the 87 surviving patients are also not mentioned.

London, W.2. S. Y. BHAGWAT.

MEDICINE IN THE NEW SOCIAL ORDER

SIR,—The views of an individual upon some topic of wide interest may owe their importance, either to the wisdom or knowledge inherent in them, or to some chance that gives them the opportunity of wielding influence upon events. Few can doubt that at present it is the latter circumstance that is commonly operative, and that such influence as opinion may exert derives more often from the authority of office than from any other single cause. Today and to a degree unprecedented in the modern history of our country, whoso possesses this order of authority may enforce his views upon an ever-increasing proportion of the community and of that community's activities. We may deplore this authoritarian trend but we cannot deny its dominance.

With all respect to its learned author, I submit that this is the consideration which lends an almost sinister importance to the lecture published in your last issue by Sir Francis Fraser over his title of Director of the British Postgraduate Federation. We cannot regard these as the views of a private individual, and hence they cannot fail to interest his colleagues, and in particular those who will share the responsibility for such success as may attend the Federation. What is the encouragement that he offers us?

Sir Francis leaves us in no doubt as to the school of opinion to which he belongs, for he tells us that

> "People are no longer as free as they were to decide the way they live and the contribution which each makes to the group or to the nation. They must submit to controls. . . . There is evidence that the Government departments concerned with recent legislation and responsible for the numerous regulations and directions that have been issued for the administration of the new Acts are fully conscious that the people require guidance to enable them to adjust their lives to the new order.

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Large numbers of inspectors from the various ministries and departments, information bureaux, resettlement officers, health visitors, almoners, social workers, and so on, are being appointed to ease the difficulties of personal readjustment. Will they not suffice? Is there need for doctors also to concern themselves with these matters? I am confident there is. . . ."

This is the new version of domestic peace in our time. As we read this artless and revealing exposition of what is designed for us by our rulers, with its operative words "controls" and "inspectors," those of us who yet retain our faith in the natural process of social evolution which has been the characteristic of the English genius, which has gained for us such liberties as we enjoy, and is so nobly exemplified in the Common Law, a chill must envelop our hearts.

We ask if this is what British medicine is to come to at the end of its long tradition of intellectual and personal freedom, for we also are only "people" and subject in our turn to controls and inspections.

Our destiny it seems is to be recruited to the ever-growing legions of controllers and inspectors in the pay of the omnipotent State, and we are to join in shepherding the mass of our fellow citizens, lumped together almost contemptuously as "people."

True, Sir Francis seeks to gild the pill by extolling what the doctor was in the past, and exhorts us so to remain; but if he is a realist at all he must well know that we can never again become the counsellors, guides, the almost pastors of our patients now that we are prejudiced in their eyes by becoming public officials engaged in one of the many aspects of "control" and "inspection."

I cannot properly use your columns, Sir, to expand this theme as it deserves. Indeed, only the insight and the eloquence of an Edmund Burke could adequately indict this arid and retrograde philosophy. I must confine myself to such reflections as come to me as a teacher of medicine, soon to be called upon, perhaps, to undertake some modest rôle in postgraduate education under the banner to which Sir Francis asks us to rally.

My theme is this: some of us have not that unquestioning faith in the powers of the individual reason—whether that of the modern politician, or that of some controller in a more restricted field—which would lead us blindly to accept only what is deliberately designed for us; or to reject out of hand anything that is not deliberately designed or wholly intelligible to the individual reason.

We know that much that is best in our social order has been the unforeseen and unintended fruit of individual genius and action, and that many institutions which rank amongst our highest achievements have arisen and continue to function without an overruling and directing mind, and again we cite the Common Law by way of example. Further, we have our experience of controllers and planners with their vast schemes for regimenting the community for its own good as they conceive it, and we have found little reason to believe that they possess some higher order of rationality, some deeper insights or sources of wisdom, a better historical sense or greater idealism than any one of us may, under Providence, enjoy.

We even doubt their invariable success in achieving the ends they propose to us—and for us—at such vast expenditure of men and money, and we find the incessant showers of leaflets that descend upon our heads from the high places, where these supermen think their great thoughts and cherish their large ambitions, conspicuous neither for clarity nor for good sense.

We continue to believe that in medicine high-level external organisation is wholly bad, that planning on any level is but a means to an end, and that it should be kept in its due place which is not the first place. We favour that true individualism so clearly defined by Lord Acton, and believe that only under its aegis can medicine flourish and advance, whether we think of it as a discipline or as a service to the community.

That we should now be invited to scorn delights and live laborious days in educating medical students, whether undergraduate or postgraduate, for no higher end than that they may become submissive cogs in a compulsive socialised order, and to become part-guardians of that vast day-nursery which some envisage as the ideal of social progress, is surely too much to ask. I am reminded of the famous closing words of poor Mrs. Ramsbottom in that engaging fable, "Albert and the Lion":

> "What, spend all my days rearing children
> To feed ruddy lions, Not me!"

The hope of British medicine is that those who will teach it may aim at some higher ideal than that expounded for them by the Director of the British Postgraduate Federation, that Athens and not Sparta will remain their intellectual home, and that those they educate may not be willing to fill the truly ignoble rôle he destines for them.

London, W. F. M. R. WALSHE.

PREFRONTAL LEUCOTOMY

SIR,—It was a pleasure to read the article of Jan. 15 by Dr. Strröm-Olsen and Dr. Tow—one of the first that has given a well-balanced and painstakingly accurate review of the long-term results of leucotomy. There is no question but that this operation has been performed in a rather indiscriminate fashion; perhaps this is inevitable when a new form of treatment is accepted too enthusiastically, but certainly there is now not the slightest justification for the operation being performed "as a routine." Its only indication is in carefully selected chronic cases in which every other form of treatment has been thoroughly tried without success.

It would be interesting to know whether in fact the three illustrative cases described by the authors had received adequate courses of electroconvulsive therapy or some other treatments before it was decided to resort to leucotomy.

Park Prewett Hospital, Basingstoke. I. ATKIN
Physician Superintendent.

Parliament

Working of the National Health Service Act

ON the motion for the adjournment in the House of Commons on Jan. 21, Sir HENRY MORRIS-JONES called attention to anomalies which had arisen in the working of the Act. Many medical men, he said, were unhappy about their present position. In the large industrial areas doctors had on the whole gained in remuneration—sometimes by as much as 25–30%—but in other places—residential, rural, and seaside resorts—their earnings had decreased to an extent which affected their morale and working power. The whole basis of remuneration, he suggested, should be reconsidered. There was much to be said for payment per attendance, with power by the State to make a grant-in-aid. He thought that the basic salary was working very badly. The distribution of doctors had been made infinitely worse by the Act, because they were now frozen in their areas. Many specialists were also finding their incomes had been drastically reduced. With the doctors' coöperation, Sir Henry ended, the Act had a wonderful future. But if the doctors were to be put in a state of financial anxiety, wear, and worry, their interest in their work might go. The Act and the health of the people would suffer in consequence.

Mr. FREDERICK MESSER, in day-to-day experience of the administration of the service, had found complete coöperation from every section of the medical profession. It was not fully realised what a tremendous task it was to pull together the small units and make a comprehensive unified service of a lot of scraps and pieces. Six months was not time enough in which to test it. We were going through a period when we were compelled to experiment with compromises, and he suggested that the negotiations that preceded the Act, in which compromises had to be reached, were responsible for much of the present difficulty. By the very nature of the service, he continued, doctors were compelled to work much harder than before. That was not a weakness of the service but a recognition of the fact that the wives and children of insured men could now get treatment. Turning to the financial side of the scheme, he pointed out that we must not be content to say the expenditure was enormous without having regard to where the money went. All those who received free treatment were receiving an addition to their income. Mr. Messer

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thought we should find that we had launched a service which is probably the finest monument to the ability of the people to meet the needs of the people.

Mr. HUGH LINSTEAD had always thought that the Act attempted to go too fast and too far, but he admitted the service was on the rails and moving, though it was creaking and groaning. He asked the Ministry for rapid action to help it run more smoothly. When, for instance, was the amending Bill to be produced? Could not the capital side of hospital finances be put on a quinquennial basis so that the committees knew more clearly where they stood? Mr. Linstead also drew attention to the difficulties which the hospital management committees faced through the activities of the nursing agencies. On qualifying, nurses joined the agencies, and then returned to the hospitals, where they were paid twice as much as the Rushcliffe scales, while the agencies collected 12½% for doing nothing at all.

Dr. HADEN GUEST stressed that when speaking of the abnormal cost of the service we must remember the enormous saving which had already begun to accrue in the improvement in health of the people. He also stressed that the doctors in industrial areas who were receiving a higher remuneration included the larger part of the general practitioners of the country. As chairman of the Medical Priority Committee his chief headache was the provision of specialists. There were not enough in the country, and he had no doubt that the question of their remuneration would be solved when the Spens Committee report was applied, as it would be.

Mr. RALPH ASSHETON asked whether the medical profession was not finding itself so overworked that doctors had not sufficient time for the treatment of serious illness. He would like to be assured that the available hospital beds were being allotted to the patients who most needed treatment. Was it not possible to give the doctors more help with non-medical work?

Mr. L. J. EDWARDS, parliamentary secretary to the Ministry of Health, said there was no longer any doubt that the new health service had been welcomed and used by all classes of the general public to an extent which exceeded expectations. The need for the service had been underestimated. In the family practitioner service, some 40 million people in England and Wales had placed their names on doctors' lists. This represented between 95 and 98% of the population. A 3% margin of error was allowed for. Of 21,000 general practitioners, 18,165 had come into the scheme. They had prescribed 75 million medicines or appliances since the service began. Of 10,000 dentists in general practice 8988 had joined the scheme, and they had treated 2,200,000 patients. A further 1,200,000 patients were under treatment at present. It looked as though the initial peak demand for dentists' services had passed, but the demand was still running at the rate of over 130,000 patients a week. Over 2½ million people had had their sight tested and over 3 million pairs of glasses had been ordered. The pent-up demand had been greater than expected. Now the rush was beginning to subside the Ministry was reviewing every side of the service.

The arrangement by which the bulk of the doctor's fee was to be paid in the form of so much per person on his list was made at the request of the profession. Payments to doctors from the appointed day to March 31 next were estimated at £32½ million, in addition to which there were Exchequer superannuation contributions amounting to £1,600,000. That over-all amount, Mr. Edwards believed, would be ample to secure that doctors would be remunerated in accordance with the recommendations of the Spens Committee. All necessary adjustments would be taken into account at the end of March. He accepted the view that the distribution had been uneven, but so far it had been on a provisional basis. He recognised that the position of the rural doctor was particularly difficult, but the new mileage arrangements should benefit him. The full effect of maternity fees had not yet shown itself in the doctor's remuneration. When the final payments were made for the period July 5 to March 31 we should see whether the remuneration of the general practitioner did accord with the Spens recommendation. If it did not the arrangements would be reviewed to see what adjustments were necessary to give effect to those recommendations.

Referring to the basic salary, Mr. Edwards pointed out that the Minister had done what the profession wanted him to do and the Government could not take the responsibility. If there was anything wrong it was for the profession through their association to tell the Government that they had begun to alter their minds. The basic salary had been granted in over 1000 cases.

Turning to the distribution of doctors, Mr. Edwards said that since July 5, 530 doctors had died or resigned and 532 new doctors had been admitted. Of these vacancies 230 were filled by a partner, assistant, or logical successor. In 238 cases no successor was thought necessary. The remaining 62 were advertised. It took 2½–3 months to fill a vacancy. So far only 2 areas —Chester and Hastings—had been completely closed, though small parts of other districts had been closed. The Medical Practices Committee were now studying reports from all executive councils.

The amending Bill was in preparation, but Mr. Edwards could not say when it would be introduced. There had been long delays for hospital beds before the appointed day. They still existed, and he asserted that beds should be allocated by medical need. No urgent case should be by-passed by less urgent cases in any accommodation, whether private or pay block. In conclusion, he added, sections of the medical profession were much overworked at present. He wished it were possible to give them some help. The scheme would succeed or fail according to the degree to which we obtained the skill and devotion of the people who work it. So far he had been pleased by their coöperation and he looked forward to improving the scheme, which was still young.

QUESTION TIME

Supply of Spectacles

Mr. PETER FREEMAN asked the Minister of Health whether he was aware that citizens of Newport had to wait for eyeglasses as long as 17 weeks; and whether he would accelerate delivery.—Mr. ANEURIN BEVAN replied: I am aware that there are difficulties generally. All practicable steps are being taken to arrange for increased production. Mr. FREEMAN: Is the position improving or getting worse?—Mr. BEVAN: The position is improving, certainly. A very large number of persons have had spectacles who formerly would not have had them.

Colonel M. STODDART-SCOTT: Will the Minister say how long it will be before children can be issued with splinterless glasses which they had prior to the Act?—Mr. BEVAN: I am sure parents would not wish to restore children to the situation in which they were before the Health Service was introduced. The question of splinterless glass where medically necessary, for example in epileptic cases, is being urgently considered.

X-ray Films

Mr. R. A. CHAMBERLAIN asked the President of the Board of Trade whether he would increase the supply of X-ray films available to hospitals, in view of the increased demand coupled with decreased supplies for home consumption.—Mr. HAROLD WILSON replied: Supplies of X-ray film to the home market have been increasing, but not enough to meet the increased demand since the war, and especially the last six months. Manufacturers have been doing all that they can to increase production, and after consultation with the Minister of Health I am asking them to supply a larger proportion of their output to the home market. There is, however, a shortage of X-ray film, not only here but throughout the world, and doctors, hospitals, and all others who use it are asked to exercise the utmost economy.

Agene

Sir ERNEST GRAHAM-LITTLE asked the Minister of Food whether he was aware that the use of 'Agene' for bleaching flour provided for human consumption has been prohibited in the U.S.A. in accordance with the advice tendered by the Food and Drug Administration; and what steps he was taking to prevent the use of agene in this country.—Mr. STRACHEY replied: I am aware that the use of nitrogen trichloride is to be discontinued in the U.S.A. on Aug. 1 next. As I informed the House on Dec. 13 a small scientific committee under the chairmanship of Sir Wilson Jameson, chief medical officer of the Ministry of Health, has been set up and is at present reviewing the results of experimental work on flour improvers now in progress in the United Kingdom and the data submitted in evidence at Washington.

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Obituary

CHRISTOPHER FRANK GOOD

C.B., M.R.C.S.

Dr. Good was a student at the London Hospital when the first world war began. At first he served as a dresser with a Red Cross unit, but later he obtained a commission in the Buffs. In 1917 he received a severe gunshot wound of the chest, and he was demobilised the following year. He returned to the London Hospital and qualified in 1919.

After a series of house-appointments at the London and a short period with the Ministry of Pensions, he settled in private practice in Battersea and there built up the experience which was to prove so valuable to his profession and to the Ministry of Health later in his career. In 1931 he entered the Ministry as deputy regional medical officer. He was promoted regional medical officer in 1937, divisional medical officer in 1940, and principal medical officer in 1946, when he succeeded Dr. Whitting in charge of the insurance medical staff.

During his years with the Ministry Dr. Good gained experience in many branches of the department's work. Early in the war he was hospital officer and later principal regional medical officer in the North-East region. When, in 1945, the insurance regional medical service was revived, he was responsible for its reorganisation. By this time, discussions on the National Health Service were in full swing and Good played an important part in them. For the last few years his hold on life had been precarious; but he stuck to his work with great courage and cheerfulness and conducted some of it from his bed in hospital.

"From my first day of service in the Ministry," writes A. L. B., "Dr. Good helped me with advice and encouragement, and, in common with all the younger men in the Ministry, I quickly learned the value of his friendly, shrewd, and tactful comment. In manner he was frank, unassuming, and imperturbable. But his apparent casualness hid a faculty for always being on the spot, both physically and mentally, at the right moment. Perhaps the best comment I can make on his life is that his loss is mourned in the Ministry by every officer—administrative, professional, and technical."

The value of Dr. Good's experience and advice were recognised in 1948 when he was appointed C.B. He died on Jan. 16 at the age of 56, and he leaves a widow.

ALBERT ERNEST HODGSON

M.D. EDIN., D.P.H.

Dr. A. E. Hodgson, until 1946 medical superintendent of the Fazakerley Isolation Hospital, Liverpool, died at his home in Maghull on Jan. 2 at the age of 68.

Born at Redcar in Yorkshire, he obtained his M.B. at Edinburgh in 1903, and three years later took the D.P.H. at Cambridge. He received his M.D. degree with commendation in 1911. His first appointment with the Liverpool Corporation, which he served for nearly 40 years, was that of resident medical officer at Mill Lane Isolation Hospital in 1907; later he was for 15 years principal resident medical officer at the Fazakerley Isolation Hospital, and in 1934 he was promoted to the post of medical superintendent there which he held until he retired.

During the 1914–18 war he served with the R.A.M.C. in India and Salonika; and was for a time officer-in-charge of the North Wales area bacteriological laboratory and cerebrospinal centre.

A colleague writes: "Hodgson was a thick-set little man, with a gentle voice and a quiet smile which mirrored an old-world courtesy, an engaging modesty, and an abundant kindness. He was outstanding in his own specialty of infectious diseases, and though this was recognised by his university appointment as lecturer in the subject, he probably got even more pleasure out of the innumerable occasions on which his local colleagues turned to him for advice about their own children, or sought his help in some obscure and difficult case. He had a wide experience of anthrax, living as he did in a port which imported hides from all over the world, and on this subject he wrote several authoritative papers. It was like him not only to set out the best lines of specific treatment, based on his own experience, but also to call attention to the anxiety neurosis which so frequently and understandably follows a serious attack of anthrax. It is also in keeping that he was a devoted and skilled follower of Izaak Walton. The loss of his wife, a sister of Prof. P. S. Lelean of Edinburgh, robbed his retirement of much of the joy which he deserved, and which his many friends would have wished for him."

HARRY STACK SULLIVAN

M.D. MARYLAND

Professor Sullivan, who died in Paris on Jan. 14, aged 56, brought a brilliant intellect to the problems of mental health. His widely ranging mind had travelled far from the study of schizophrenia, to which he made valuable contributions in his earlier years, to the larger and more urgent study of the requirements for harmonious group life. He studied at Chicago and the University of Maryland, where he graduated in 1924. As professor at Georgetown University, Washington, he was chairman of the council of fellows of the Washington school of psychiatry, and he was editor of the journal *Psychiatry*. During the late war he became consulting psychiatrist to the U.S. Army Office of Selective Service and bore much responsibility for the significant developments there in methods of personnel selection. Later he worked as a psychiatric consultant in the American zone of Germany.

Dr. Sullivan was deeply convinced of the need for a "multi-disciplined" approach to the problems of international, national, and community life, and he was the originator of the international preparatory commission, consisting of psychiatrists, psychologists, sociologists, anthropologists, economists, clergy, and lawyers drawn from as many countries as possible, which made so important a contribution to the work of the International Congress on Mental Health held in London last August. Pursuing these aims, he returned to Europe in January to attend the meeting in Amsterdam of the executive board of the World Federation for Mental Health as a member of its advisory interprofessional committee. He was actively engaged in promoting schemes, proposed by the federation, for the scientific training in human relations of those already engaged in international work, and he went on from Amsterdam to Paris to help UNESCO in a conference on an allied project.

Unfortunately these journeys proved too great a strain on a heart which had given him serious trouble for some years. His sudden death during his mission was a fitting end for a single-minded man who inspired devotion among his immediate colleagues and students. He was a pioneer among those who have carried psychiatry from its preoccupation with morbid processes into a wider study of individual and group living.

JOHN HENRY COSTE

F.R.I.C., F.INST.P.

Mr. J. H. Coste, chemist-in-chief in the public-health department of the London County Council from 1913 to 1936, died at his home at Smallfield, Surrey, on Jan. 3. Born in 1871, he was educated at Finsbury Technical College, and, after a few years spent in the laboratories of J. A. Voelcker at the Royal Agricultural Society, Coste was appointed to the staff of the chemical and gas-testing department of the L.C.C. in 1894. Later he became chief assistant, a post which he held till he became chemist-in-chief in 1913.

As a chemist Coste had many interests, and his papers on applied research ranged over paint composition, turpentine, examination of petroleum mixtures (under the Statutory Acts), and viscosity of lubricating oils. He was the author of a book on the calorific power of gas and part author of two others on paint and paint pigments and on fuel. As official agricultural analyst for the County of London he was also concerned with all scientific aspects of agriculture. The London County Council's responsibility for the disposal of the sewage of London is shared between the chief engineer's and public-health departments, and in this task Coste was a worthy successor to W. J. Dibdin, a pioneer in the development of the sewage treatment process on a scientific basis. He also took a realistic interest in rural water-supplies; in his Chadwick lecture of 1933

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he proposed that where there was not piped water in every house a public supply should be placed in a water-house or hydrarium where there would be baths and facilities for laundering. Probably the activity which most appealed to him in his later years was his work for the measurement and abatement of atmospheric pollution. For many years he was a member of the Atmospheric Pollution Research Committee, and he kept up his interest in this subject until his death. A kindly man, he was always willing to help his colleagues, and for many years he advised THE LANCET on problems in the field where chemistry marches with medicine.

Appointments

NEWNHAM, C. T., M.R.C.S., D.O.M.S.: asst. M.O., Paddington, British Railways Western Region.

London County Council:

Asst. M.O. in public-health department:
BACH, LORNA, M.R.C.S., D.P.H.
HADAWAY, STELLA, M.B. Lond., D.P.H.
MACMILLAN, SYLVIA, M.B. Lond., D.P.H.
MOSS-MORRIS, SHEILA, M.B. Witwatersrand, D.C.H.
ROBERTS, PEGGY, M.R.C.S.
WILLIAMS, LLARY, M.B., B.SC., Wales, D.P.H., D.C.H.

Colonial Service:

BROWN, A. J., D.S.O., M.R.C.S.: M.O. (Out Islands), Bahamas.
COOPER, W. F., M.B. Camb., D.P.H.: port M.O., Aden.
CRUIKSHANK, J. M., O.B.E., M.D. McGill, F.A.C.S., D.P.H.: director of medical services, Fiji, and inspector-general of South Pacific Health Service.
KOTOWSKI, J., M.B. Polish School of Medicine: M.O., Falkland Islands.
MCSHINE, L. A. H., M.B. Lond., F.R.C.S.: M.O., grade B, Trinidad.
MICHALSKI, EDWARD, M.D. Warsaw: M.O. (district services), Trinidad.
NORMAN-JONES, MARY, M.A., M.B. Camb., D.P.H.: M.O., Uganda.
POTTINGER, J. H., M.B. Lpool, D.T.M., D.T.H., D.P.H.: asst. director of medical services, Nigeria.
RENNER, E. A., O.B.E., M.B. Edin.: asst. director of medical services, Sierra Leone.
SILVERA, W. D., M.B. Edin., M.R.C.P.: senior lecturer on pathology, University College, Ibadan, Nigeria.
YOUNGLAO, L. P., M.B. N.U.I., D.T.M. & H.: senior M.O., British Honduras.

Births, Marriages, and Deaths

BIRTHS

ADAMS.—On Jan. 16, in London, the wife of Dr. Michael Adams—a son.
BALLANCE.—On Jan. 18, the wife of Dr. G. A. Ballance—a daughter.
CORBIN.—On Jan. 18, the wife of Dr. H. P. F. Corbin—a son.
MATHERS.—On Jan. 17, in Glasgow, the wife of Dr. J. R. Mathers—a daughter.
OGILVIE.—On Jan. 7, in London, the wife of Dr. A. C. F. Ogilvie—a daughter.
PINNIGER.—On Jan. 12, at Otahuhu, New Zealand, the wife of Dr. J. L. Pinniger—a daughter.
PRICE.—On Jan. 4, the wife of Dr. H. C. Price—a son.
STEIN.—On Jan. 17, in London, to Dr. Lore Stein, wife of Mr. G. E. Stein, F.R.C.S.—a daughter.
STEVENS.—On Jan. 14, the wife of Dr. C. P. Stevens—a daughter.
WALTERS.—On Jan. 15, at Lincoln, the wife of Mr. G. A. B. Walters, F.R.C.S.E.—a daughter.

MARRIAGES

EVANS—BRICKLE.—On Jan. 15, in London, Robert J. Evans, M.B., to Muriel Brickle.
NUNN—KELLY.—On Jan. 18, in London, J. L. Nunn to Joan Hazel Kelly, M.B.

DEATHS

BAILEY.—On Jan. 16, at Victoria, B.C., Kenneth Norman Grierson Bailey, M.B. Lond.
FIELDEN.—On Jan. 23, Edward Fielden, M.B. Durh., aged 77.
FORSTER.—On Jan. 16, Arthur Graham Foljambe Forster, M.D. Edin., aged 79.
FRERE.—On Jan. 15, at Fleet, Hants, John Edward Frere, M.A., M.B. Camb.
GOOD.—On Jan. 16, Christopher Frank Good, C.B., M.R.C.S.
JORDAN.—On Jan. 19, at Wroughton, Wilts, John Herbert Jordan, M.C., B.A., M.B. Camb.
KAY.—On Jan. 16, at East Grinstead, Alfred Reginald Kay, B.A. Oxfd, M.R.C.S., aged 79.
RYLES.—On Jan. 14, at Hoylake, Cheshire, Charles Sydney Ryles, O.B.E., M.B. Edin., D.P.H., colonel, R.A.M.C., retd, aged 65.
STOREY.—On Jan. 16, in London, Percy Arthur Storey, M.D. Durh., aged 79.
THOMAS.—On Jan. 21, at Parke, Whitland, Carmarthenshire, Rowland Lewis Thomas, L.M.S.S.A., D.P.H., aged 84.
WELLS.—On Jan. 17, at Stratford-on-Avon, Philip Hewer Wells, M.C., M.R.C.P., aged 56.
WILD.—On Jan. 5, in London, Granville Burnett Wild, M.B. Manc., lieut.-colonel, R.A.M.C., aged 57.
WILSON.—On Jan. 21, at Hove, Louise Whitman Farnam Wilson, M.D. Yale.

Notes and News

NEW LIGHT ON PLANT NUTRITION

"IN the later part of the last century, scientific biological departments built walls around themselves attempting to become self-contained. In late years it has been the ambition of most workers to break down these entirely artificial barriers to interchange of ideas." Having the curiosity proper to a scientist, Dr. A. E. Barclay has applied his technique of micro-arteriography[1] to examining the leaves of plants, and with a botanical colleague, Mr. Donald Leatherdale, he reports some unexpected findings which may well prove important.[2] Radiographed with soft X rays, the leaves show multitudinous minute radio-opaque objects ("spots"), usually distributed along the veins, although a few may lie in the intervenous areas. These spots, composed of material with atomic weights higher than those of the surrounding tissues, are of fairly uniform sizes in each species of plant but differ in different species: in the rose two sizes are found (about 150 μ and about 250 μ) while in prunus there are three (100 μ, 200 μ, and 500 μ). The spots are numerous during spring and early summer, and it is thought that they may be stores of nutrient material on which the leaf draws as needed. Barclay and Leatherdale assume that they travel from the roots to the leaves, though apparently the direction of their movement has not yet been actually proved. The question is raised whether similar spots might be found in animal tissues.

University of Oxford

On Jan. 20 the honorary degree of SC.D. was conferred on Lieut.-General Sir William MacArthur.

University of London

Mr. A. Ll. Hodgkin, F.R.S., will give two lectures on Ionic Exchange and Electrical Activity in Nerve and Muscle, at St. Thomas's Hospital medical school, London, S.E.1, at 5 P.M. on Thursdays, March 3 and 10.

University of Manchester

Mr. W. I. C. Morris has been appointed whole-time professor of obstetrics and gynæcology in succession to the late Prof. Daniel Dougal. He will take up his duties in the summer.

Mr. Morris graduated at Edinburgh in 1930, with honours in medicine and surgery, and was awarded the Beaney prize in anatomy and surgery and the James Scott scholarship in obstetrics. After a period in general practice, he was in 1933 appointed obstetrical house-surgeon in the Royal Maternity and Simpson Memorial Hospital, Edinburgh, where he was resident obstetrical officer for the next three years. He became F.R.C.S.E. in 1934 and M.R.C.O.G. in 1937, in which year he was appointed as the first whole-time obstetrician and gynæcologist to the Ayr county council. He held this post until 1946 with an interruption of four years' military service. Holding a Territorial commission, he was embodied in 1939 and posted to Gibraltar as D.A.D.M.S. Since 1946 he has been senior lecturer in obstetrics and gynæcology in Edinburgh University, and obstetrician and gynæcologist to the Western General Hospital. His principal research has been on radiological pelvimetry.

Royal College of Surgeons of England

The college and the Institute of Child Health are holding a joint course of lectures and clinical conferences on the Surgery of Childhood from July 4 to 8. Further particulars will be found in our advertisement columns.

Faculty of Homœopathy

On Thursday, Feb. 3, at 5 P.M., at the Royal London Homœopathic Hospital, Great Ormond Street, W.C.1, Dr. F. H. Bodman will give an address on Homœopathy and the Psychosomatic Approach.

Royal Society

At a meeting of the society to be held at Burlington House, Piccadilly, London, W.1, on Thursday, March 10, at 4.30 P.M., Sir Charles Harington, F.R.S., will speak on the work of the National Institute for Medical Research, of which he is director.

Priority Milk for Sick Children

On the recommendation of his medical advisers the Minister of Food has arranged for medical certificates recommending priority allowances of milk for sick children temporarily absent from school to be valid for 4 weeks instead of 1 week as at present.

1. *Brit. J. Radiol.* 1947, **20**, 394.
2. *Ibid*, 1948, **21**, 544.

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North Persian Forces Memorial Award

Dr. J. N. P. Davies has been awarded the North Persian Forces Memorial Silver Medal for 1947 for his paper on the Pathology of Central African Natives, which was published in the *East African Medical Journal*.

Civilian Sick in Service Hospitals

In a circular to hospital authorities the Ministry of Health points out that Service hospitals are always prepared to admit civilian emergency cases, and, so far as their resources permit, selected non-urgent cases. Regional boards are asked to consider extension of this arrangement, which is one means of reducing waiting-lists.

Swiney Prize for Medical Jurisprudence

The prize for 1949 has been awarded, on the recommendation of a joint committee of the Royal Society of Arts and the Royal College of Physicians, to Prof. John Glaister for his book *Medical Jurisprudence and Toxicology*. Professor Glaister also received the prize, jointly with Prof. J. C. Brash, in 1939.

Royal Sanitary Institute

The presidents of the sections of the Health Congress, which is to be held at Brighton from May 23 to 27, will include: Prof. Andrew Topping (preventive medicine); Prof. W. S. M. Craig (maternal and child health); Prof. P. A. Buxton, F.R.S. (tropical hygiene); and Prof. T. Ferguson (hygiene in industry).

British Schools Exploring Society

An honorary physician and an honorary surgeon are wanted for the Northern Norway Expedition, leaving on Aug. 3 and returning about Sept. 14. The cost to each member will be £110 plus about 10 guineas for personal equipment. Application should be made as soon as possible to the hon. secretary, White Barn, Old Oxted, Surrey.

Retirement from the L.C.C. Service

Dr. J. Nairn Dobbie, a senior medical officer in the public-health department, has retired from the service of the London County Council.

Dr. Dobbie, who served in the R.A.M.C. from 1914 to 1919 and was twice mentioned in despatches, joined the L.C.C. in 1921, his work including inquiries into the health of school-children and the supervision of the council's rheumatism scheme from its inception in 1926. From 1930 he assisted in the administration of special hospitals transferred under the Local Government Act, 1929; and after promotion to senior medical officer in 1934 he was concerned with the structural improvement of hospitals. He was seconded in 1938 for duty with the Ministry of Health in connexion with the E.M.S., and during the early years of the war acted as hospitals officer for London. He returned to the L.C.C. in 1941 as senior medical officer in immediate charge of the school health service.

World Health Organisation

Dr. Norman D. Begg, who has been appointed acting director of the W.H.O. Special Office for Europe, states that requests for assistance in the form of advisory and demonstration services, fellowships, medical literature, and other supplies and equipment have already come from Albania, Austria, Belgium, Bulgaria, Byelorussia, Czechoslovakia, Finland, France, Greece, Hungary, Italy, Netherlands, Norway, Poland, and Yugoslavia. These requests "amount to just about twice as much for 1949 as the W.H.O. budget for the current year will permit." The office, located at Geneva, will work in close liaison with other sections of the W.H.O. secretariat, particularly the medical supply section of which Dr. Chang-Yui Shu has been appointed chief. One of the critical problems is the widespread shortage of penicillin. A survey is being made of the penicillin plants supplied by UNRRA to a number of European countries but not functioning at present; and it is hoped that if some of these plants can be put into operation an important step will have been taken toward the success of the large-scale anti-syphilis programmes now under way—with W.H.O. technical assistance and with supplies being furnished by UNICEF—in Poland, Bulgaria, Finland, Hungary, and Yugoslavia. Preliminary work for similar campaigns is now being done in Italy and Czechoslovakia.

Dr. Begg, formerly medical superintendent of the Eastern Hospital (L.C.C.), worked in Warsaw for UNRRA and has since been chief of the W.H.O. Poland mission.

Dr. Shu has served with the Chinese ministry of health, and represented his country as technical expert on the Chinese delegation to the World Health Assembly.

Association of Clinical Pathologists

A meeting of this society began at the Westminster Hospital, London, S.W.1, on Jan. 27, and will continue today, Jan. 28, and tomorrow.

Protection against Radiation Hazards

The 7th revised report of the British X-ray and Radium Protection Committee contains recommendations for protection against irradiation apart from that due to radioactive isotopes, which is dealt with in the *Introductory Manual on the Control of Health Hazards from Radioactive Materials*, prepared for the Medical Research Council by the Ministry of Supply, Atomic Energy Research Establishment. Copies of the report and the manual are obtainable from the hon. secretaries of the committee at 32, Welbeck Street, London, W.1.

Notification of Incapacity

The Ministry of National Insurance points out that payment of sickness benefit may be delayed or lost if people who are sick fail to notify the local National Insurance office of their incapacity within 3 days. If for any reason a medical certificate cannot be obtained within this time, a note giving the full name, address, and National Insurance number should be sent by the claimant, or if he cannot send it by someone on his behalf, to the local National Insurance office informing them of the incapacity. This should be followed by the first medical certificate as soon as possible and in any case within 10 days.

The Wollaston medal of the Geological Society has been awarded to Dr. Robert Broom for his researches in vertebrate palæontology, especially in the study of the evolution of the reptiles and of the anthropoid apes and man.

Dr. W. J. O'Donovan has been adopted as prospective Conservative candidate for Fulham West, at present represented by Dr. Edith Summerskill. Dr. O'Donovan was M.P. for Mile End from 1931 to 1935.

Captain B. J. Fowler, R.A.M.C., surgeon at the military hospital in Tobruk, has been appointed chevalier of the Legion of Honour by the President of the French Republic, in recognition of valuable services rendered by him on the occasion of a mine explosion in April, 1947.

Diary of the Week

JAN. 30 TO FEB. 5

Tuesday, 1st

UNIVERSITY COLLEGE, Gower Street, W.C.1
5.15 P.M. (Physiology theatre.) Dr. E. Ashworth Underwood: Digestion and Metabolism. (Second of four lectures.)

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. W. N. Goldsmith: Lupus Erythematosus.

Wednesday, 2nd

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Mr. Terence Cawthorne: Pathology and Surgical Treatment of Labyrinthine Vertigo of Non-infective Origin. (Hunterian lecture.)

Thursday, 3rd

LONDON COUNTY MEDICAL SOCIETY
4.30 P.M. (Mile End Hospital, Bancroft Road, E.1.) Dr. A. F. Mohun, Dr. J. Ruble: Streptomycin in the Treatment of Tuberculosis.

INSTITUTE OF DERMATOLOGY
5 P.M. Dr. G. B. Mitchell-Heggs: Drug Eruptions.

ROYAL PHOTOGRAPHIC SOCIETY, 16, Prince's Gate, S.W.7
7 P.M. *Medical group.* Detective-Inspector P. G. Law: Forensic Photography.

Friday, 4th

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. E. H. Hudson: Differential Diagnosis of Carcinoma of Lung.

MAIDA VALE HOSPITAL, W.9
5 P.M. Dr. P. H. Sandifer: Clinical demonstration.

ST. GEORGE'S HOSPITAL, S.W.1
4.30 P.M. Psychiatry demonstration.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh, 1
8 P.M. Mr. Rodney Maingot: Surgery of Cholelithiasis and the Complications of Operative Treatment.

Saturday, 5th

BRITISH TUBERCULOSIS ASSOCIATION
10 A.M. (Hospital for Sick Children, Great Ormond Street, W.C.1.) Dr. L. G. Blair: Radiology.
2 P.M. Dr. MacFarlane: Streptomycin Therapy in Acute Miliary Tuberculosis and Tuberculous Meningitis.

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HISTORICAL BUILDING
DES MOINES, IOWA

THE RHESUS FACTOR *

A SUMMARY BASED ON 200 CASES

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SINCE there is still considerable perplexity in the minds of many doctors about the significance of the rhesus or Rh factor, we are attempting here to summarise the subject for those who have only occasional contact with it.

The summary is based on nearly 200 cases in which anti-Rh antibodies were found. These occurred in many hospitals and were investigated at the Group Laboratory from 1942 to the end of 1946. Some cases occurring in 1947, mainly at Lewisham Hospital, are also included. Unfortunately the data on many cases are incomplete, and the clinical figures given refer only to 117 cases which have been satisfactorily investigated; nearly all of these have been seen by one of us personally. Up to 1945 most of the patients were investigated either because they had borne a child suspected of hæmolytic disease or because of a transfusion reaction, but in 1946 and subsequently a growing proportion have been identified before delivery owing to increasing routine rhesus testing of antenatal patients. The value of this earlier diagnosis is becoming more obvious now that premature induction of labour and replacement therapy are more widely practised. None of the patients in this series was treated by replacement transfusion. Our experience to date of this method shows apparent improvement on earlier figures.

SEROLOGY OF THE RH FACTOR

The Rh Antigen

It was first shown in 1940 that, if the red cells of a rhesus monkey were injected into a guineapig, antigens contained in the red cells caused the production of antibodies which would agglutinate the red cells not only of the rhesus monkey but also of about 85% of white people. The type of human red cells which were agglutinated were described as Rh-positive (Rh) and those which were not agglutinated were called Rh-negative (rh).

Agglutinins with similar specificity were soon discovered in the sera of some women who had borne infants with erythroblastosis fœtalis, and sometimes in the sera of persons who had transfusion reactions not explained by incompatibility of the A, B, O blood-groups.

It was also found that the mothers of children with erythroblastosis fœtalis were nearly all Rh-negative, and the commonest findings in such families were: mother Rh-negative; father and children Rh-positive. Similarly, in unexplained transfusion reactions, the Rh groups were commonly: patient Rh-negative; donor Rh-positive.

Family studies have shown that Rh characters obey the ordinary laws of inheritance, and each person's cells contain two of these characters, one derived from each parent. Thus the commonest combination found in families affected with erythroblastosis is: mother rh rh (homozygous Rh-negative); father Rh Rh (homozygous Rh-positive); children Rh rh (heterozygous Rh-positive).

Iso-immunisation

In the sense used here iso-immunisation means the production by a person of antibodies to some component (antigen) of the red cells of another person which is not contained in his own red cells. In clinical practice this takes place by two methods. The first is by parenteral introduction of the blood of another person, usually by blood-transfusion; but it should be noted that intramuscular injections of blood can also act as potent antigenic stimuli. The second is by the escape of small quantities of fœtal blood through the placenta into the maternal circulation. Both these methods are of clinical importance.

Rh Antibodies

The type of antibody originally found was an agglutinin which acted on a saline suspension of Rh-positive red cells and caused them to clump, but in many otherwise typical patients such agglutinins could not be demonstrated. Race, at Cambridge, and Wiener, in America, showed independently that in most of these cases an antibody was present. This antibody attached itself firmly to Rh-positive cells but did not agglutinate them, and its presence was demonstrated by the fact that the cells to which it was attached could no longer be agglutinated by an Rh-agglutinating serum. This type of antibody was called an "incomplete antibody," "blocking antibody," or "coating factor." More recently Diamond has shown that, by carrying out agglutination tests in albumin solution instead of saline solution, agglutination of Rh-positive cells will take place with both types of antibody, and it is customary now to report tests for Rh antibody as agglutination to "x-titre" in saline solution and to "y-titre" in albumin. From the practical diagnostic and prognostic points of view both antibodies have much the same significance and may coexist in the same patient.

The Coombs test is another sensitive way of demonstrating the presence of antibody. Rh-positive cells which have been acted on by a serum containing "incomplete antibody" acquire a coating of antibodies which are contained in the globulin fraction of the serum. Such cells are described as "sensitised." If these sensitised cells are thoroughly washed in saline solution, to remove all excess of serum-protein, and are then treated with Coombs serum obtained by injecting human serum-globulin into a rabbit, they are agglutinated, whereas unsensitised cells do not react with Coombs serum. This test is known as the *indirect* Coombs test.

The *direct* Coombs test is used in examining the blood of a newborn baby. The well-washed cells of the infant are treated directly with Coombs serum. If agglutination takes place it indicates that the child's cells are sensitised and that the child is likely to develop hæmolytic disease.

Rh Subgroups and Antibodies

Most of the human anti-Rh sera behaved in the same way as the original guineapig sera and reacted with 85% of human red cells, but the rapid discovery of antibodies with other specificities in cases of erythroblastosis indicated that the Rh factor was complex. Fisher's analysis, described below, clarified the situation, and the notation devised by Fisher is now practically universally used in describing Rh subgroups and antibodies.

Fisher's Theory

Fisher reasoned from the reactions of certain cells with certain sera that the Rh chromosome contained three genes, each of which could occur in either of two forms (allelomorphs). These genes he described as C,c; D,d; and E,e. Every chromosome contains one, and only one, component from each of these pairs, and common Rh arrangements are CDe, cDE, and cde. For shortness and convenience these assemblies of genes are often referred to by the names originally given by Wiener—e.g., CDe = Rh_1, cDE = Rh_2, cde = rh.

Every cell, except the germ cells, contains paired Rh chromosomes, one of which is derived from each of the parents. Each cell may contain the same, or different,

* This paper was written before the publication of the recent M.R.C. memorandum. It was nevertheless felt that this simple summary might still be of value as a general introduction to the subject.

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Rh chromosomes. For example, the Rh-negative chromosome has the genes cde, and a homozygous Rh-negative person has therefore cde on each chromosome; his genetic make-up is described as cde/cde. On the other hand, a heterozygous Rh_1 person has one Rh_1 (CDe) chromosome and one Rh-negative (cde); hence his make-up is described as CDe/cde. The germ cell contains only single chromosomes.

All these Rh genes—C, c, &c.—can act as antigens, and a woman can theoretically make antibodies to any gene she does not herself possess, if stimulated by pregnancy or transfusion; in fact, antibodies to all six antigens have now been found. D is the most important antigen. The original anti-Rh serum was an anti-D serum, and any person whose cells contain the D antigen and are agglutinated by an anti-D serum is to be regarded as Rh-positive. This serum containing anti-D is described as a standard Rh-antiserum.

The incidence of these different antibodies, however, varies enormously, and in many cases antibodies to more than one Rh gene are found. Thus in our whole series of sera from 400 patients with Rh antibodies up to date about two-thirds contained anti-D antibodies alone, and about a third anti-D + anti-C. Three sera contained anti-D + anti-E, and one contained anti-c. One serum apparently contained anti-C alone. In many of the anti-D + anti-C sera there was an antibody to C acting in saline solution, but the anti-D antibody was of the type demonstrable only in albumin.

Genotypes and Phenotypes

The terms "genotype" and "phenotype" sometimes cause difficulty. "Genotype" indicates the true genetic make-up of a person, whereas "phenotype" means the apparent genetic make-up, so far as can be ascertained with the sera available. In a few cases the genotype can be stated with certainty, but in other cases it can only be guessed at on the grounds of probability. Thus a person whose cells are not agglutinated by anti-C, anti-D, or anti-E sera has the genotype cde/cde, whereas one who reacts positively with anti-C, anti-D, and anti-c sera and negatively with anti-E may have the genotypes CDe/cde (Rh_1rh), CDe/cDe (Rh_1Rh_0), or Cde/cDe ($Rh'Rh_0$). Far the commonest of these is the first, and a person reacting in this way is often described as having the genotype Rh_1rh or as a heterozygous Rh-positive. This may be misleading, for we have records of three fathers of erythroblastotic families who gave these reactions, but were shown by family studies to have the rarer genotype CDe/cDe (Rh_1Rh_0), which is homozygous and not heterozygous so far as the important –D– antigen is concerned. Many genotypes can only be distinguished with certainty by family studies, and it is wise to be very cautious in stating that a man is homozygous or heterozygous.

TABLE I—REACTIONS TO ANTISERA C, D, E, AND c AND FREQUENCY OF COMMONEST GENOTYPES

Reactions with antisera				Common genotypes in each group		Approximate frequency %
C	D	E	c			
+	+	−	+	Rh_1rh	CDe/cde	33
				Rh_1Rh_0	CDe/cDe	3
+	+	−	−	Rh_1Rh_1	CDe/CDe	19
−	+	+	+	Rh_1Rh_2	cDE/cDE	2
				Rh_1rh	cDE/cde	10
+	+	+	+	Rh_1Rh_2	CDe/cDE	13
+	−	−	+	$Rh'rh$	Cde/cde	1
−	+	−	+	Rh_0rh	cDe/cde	2
−	−	+	+	$Rh''rh$	cdE/cde	1
−	−	−	+	$rhrh$	cde/cde	15

Other types are very rare.

The genes comprised in the various Rh chromosomes are as follows:

Rh-positive	*Rh-negative*
Rh_1 = CDe	Rh′ = Cde
Rh_2 = cDE	Rh″ = cdE
Rh_0 = cDe	rh = cde
Rh_z = CDE	Rh_y = CdE

(Rh_z and Rh_y are very rare)

Phenotypes which can be recognised by the four most generally available anti-Rh sera are shown in table I.

Importance of Rh Subgroups

Since a person can produce antibodies to any antigen he or she does not possess, it may be necessary in investigating a case of erythroblastosis or an incompatible transfusion reaction to determine the complete antigenic structure of mother and child, or of donor and recipient.

Thus, though the commonest finding is that the patient is Rh-negative (cde/cde), women of the subgroups Rh′ (Cde/cde) and Rh″ (cdE/cde) can produce antibodies to the –D– antigen which they do not themselves possess. For this reason patients of these types Rh′ or Rh″ are regarded as Rh-negative and must only receive Rh-negative blood if transfusion is needed. On the other hand, it has already been pointed out that about a third of the sera containing Rh antibodies contain anti-C as well as anti-D, and *donors* of the types Rh′ or Rh″ must not be accepted as Rh-negative; Rh-negative donors must be of the type cde/cde.

Occasionally antibodies are produced in Rh-positive women. Thus one mother of the type Rh_1Rh_1 (CDe/CDe) produced an anti-c antibody when carrying a fœtus of the type Rh_1rh (CDe/cde). Cases have been described, though we have not personally encountered one, where anti-E has been produced in an Rh_1Rh_1 (CDe/CDe) patient by a fœtus of the type Rh_1Rh_2 (CDe/cDE). Both these bloods are Rh-positive, and without determination of the subgroups concerned the mechanism of sensitisation is not clear.

Recent work has shown that the Rh factor is more complicated than Fisher's original theory suggested, and variants of the C and D genes have been identified. Their occurrence and that of iso-immunisation to factors other than Rh are of great genetic interest, and examples should be referred to special laboratories for full investigation.

All sera used for Rh testing are obtained from patients who have developed Rh sensitisation. For the work to continue it is essential for doctors concerned with such cases to provide adequate quantities of blood for the production of testing sera. Without such coöperation any extension of Rh testing will be impossible.

SENSITISATION OF WOMEN

We have met doctors who regard an Rh-negative woman as inevitably condemned to a series of stillbirths and who, in consequence, spread unnecessary alarm among them. A sense of proportion must be maintained in this matter. First of all, an Rh-negative woman with an Rh-negative husband (this includes about a sixth of all the Rh-negative women) is not at risk at all, apart from transfusion. About 12% of all marriages are between an Rh-negative woman and an Rh-positive man but less than 1 in 20 of these women have any trouble, apart from transfusion. In a year's routine testing at the Lewisham Hospital antenatal clinic, out of 147 Rh-negative multiparæ antibodies were found in 6, an incidence of 1 in 24. These occurred in a total of 1564 antenatal patients, or 1 in 260 pregnancies.

In women who have received a transfusion the probability of developing antibodies is considerably greater.

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It is extremely rare for the first child to be affected unless there has been a previous transfusion; in our series there were only 2 such cases.

Dangers of Transfusion

The risks of haphazard transfusion cannot be emphasised too strongly. They are twofold: the immediate risks to a patient whose blood already contains Rh antibodies, and the danger to subsequent pregnancies in any Rh-negative woman.

We have records of 9 cases, 2 of them fatal, where serious reactions followed the administration of Rh-positive blood to patients with Rh antibodies. It is not sufficiently realised that this danger is just as great as in cases of incompatibility of the A, B, O groups. In 6 of these transfusions the previous history of delivery of a macerated fœtus or an erythroblastotic child should have given ample warning.

As regards the risks to the fœtus, we have records of 8 cases where a transfusion had been given before the patient had borne a live child. The subsequent history of these patients shows 11 pregnancies, only 3 of which produced living children, the remaining 8 being stillborn or dying from erythroblastosis fœtalis. These tragedies could have been prevented.

There is evidence that intramuscular injections of small quantities of incompatible blood can also cause sensitisation, later manifest when the patient becomes pregnant. Under no circumstances whatever should blood be injected either intravenously or intramuscularly into a female child or woman of child-bearing age without previous Rh investigation and the use only of compatible blood.

Iso-immunisation to Other Antigens

Iso-immunisation to A or B blood-group antigens occurs so rarely in cases of erythroblastosis as to be a curiosity. It has been mentioned above that, in addition to Rh iso-immunisation, antibodies are occasionally produced to other rare types of antigen, some of which have only been found in a particular family. For this reason, in a suspected case of iso-immunisation where no ordinary antibody is found, it is desirable to send the blood of both parents to the laboratory, so that the mother's serum can be tested for any antibodies against the father's cells.

EFFECTS OF MATERNAL ISO-IMMUNISATION ON THE FŒTUS: ERYTHROBLASTOSIS FŒTALIS

Erythroblastosis fœtalis, or hæmolytic disease of the newborn, is the condition produced in the fœtus by iso-immunisation of the mother. The mechanism appears to be as follows. Small quantities of fœtal blood containing the Rh antigen escape through the placenta into the maternal circulation. If the mother is Rh-negative, antibodies are produced in her serum. These antibodies then pass back into the fœtal circulation, where they react with the Rh substance in the infant's red cells and possibly other tissue cells and cause the disease. It is extremely rare for a first child to be affected in this way; the disease usually becomes manifest only in the second or third pregnancy. The important exception is where the Rh-negative mother has received a transfusion of Rh-positive blood; as already noted, this often produces tragic results even in the first pregnancy. When once a woman has been delivered of an erythroblastotic child, subsequent children are practically always affected, unless the husband is heterozygous.

Miscarriages in the early part of pregnancy are practically never due to Rh sensitisation. Its effect usually makes itself felt in the last three months of pregnancy, and most intra-uterine deaths from this cause occur after the 32nd week.

When the fœtus dies before delivery, the commonest result is a macerated stillbirth or a dead fœtus showing hydropic changes. Usually the blood is too degenerate for examination, but Potter has shown that nucleated red cells are still to be found in the lungs after the blood in the circulation has been destroyed, and this finding may be taken as supporting the diagnosis. In both of these conditions it is common for the liquor amnii to be brownish.

In the infants who are born alive the following effects may be produced:

(1) *Hydrops Fœtalis.*—We are not aware of a case in which such an infant has survived.

(2) *Severe Icterus Gravis Neonatorum.*—In this type of case the infant develops jaundice and anæmia within a few hours of birth, has an enlarged liver and spleen, and will not usually survive more than three or four days without treatment.

(3) *The Common Type.*—In these cases a progressive anæmia is present, but the infant usually remains in good condition until the anæmia becomes severe. A moderate jaundice appears about 24–28 hours after birth and persists for about a week or more. Sometimes the jaundice is minimal, and very rarely one sees an affected child who never has manifest jaundice.

(4) *Late Anæmia.*—If the disease passes unrecognised it may lead to a very severe anæmia towards the end of the second week of life. By that time the jaundice has faded and the child is white, feeble, and drowsy. In such a weakened state it readily develops diarrhœa, and we have now seen several children born outside who were sent to hospital with a mistaken diagnosis of gastro-enteritis.

Some complications arise so early in the disease as to present as an integral part of it; these are:

(5) *Congenital Obliteration of the Bile-ducts.*—Rarely cases of icterus gravis neonatorum have an obstructive jaundice superimposed on their hæmolytic jaundice. This seems to be due to inspissated bile blocking the common bile-duct. Very occasionally fibrosis of the bile passages is the end-result, but Diamond believes that most cases of icterus gravis with persistent jaundice will recover, though the jaundice may persist for months.

(6) *Kernicterus.*—This is the most serious complication of erythroblastosis fœtalis. Most of the infants with icterus gravis neonatorum who die, other than of anæmia, do so after three or four days and at necropsy are found to have yellow staining of the basal ganglia and subthalamic, mid-brain, and hind-brain nuclei. These children usually show involuntary movements, commonly of extension and sometimes repetitive; neck-rigidity, head-retraction, or even opisthotonos; and alternating states of muscular rigidity and flaccidity. Grunting respiration is not uncommon, and the skin colour suggests that there is peripheral circulatory failure. Sometimes, however, one sees a child with icterus gravis who has slight neck-rigidity without other signs of cerebral disturbance. In such cases a guarded prognosis should be given, since a spastic diplegia may develop later, as it may rarely in children who have never previously shown evidence of nervous damage.

(7) *Purpura* and hæmorrhagic disease of the newborn are practically never manifestations of Rh iso-immunisation. We have met one case where purpura developed, but it responded to vitamin K, and the mother had a prolonged prothrombin-time, so the purpura was presumably merely coincidental.

DIAGNOSIS OF ERYTHROBLASTOSIS FŒTALIS

The diagnosis of erythroblastosis fœtalis may be obvious in the fully developed case with well-marked jaundice, progressive anæmia, and a large excess of nucleated red cells, but the diagnosis should be made without waiting for these symptoms to develop, especially if the full value of replacement transfusion is to be obtained.

The diagnosis of erythroblastosis fœtalis from physiological jaundice can only be made with certainty by the direct Coombs test on the infant's cells. This can be done on the cord blood of the newborn infant or on cells obtained by skin puncture. If the Coombs test is positive the child's cells are sensitised through having been acted on by some antibody, though the nature of the antibody is not disclosed by the test. The presence of "free

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antibody" in the Coombs-positive infant's serum often indicates a severe affection. Clinical jaundice usually comes on earlier and is more intense in erythroblastosis fœtalis than in physiological jaundice, but the variation from case to case is so wide that this difference is unreliable for differential diagnosis. The Coombs test may remain positive for several weeks.

The apparent Rh group of the newborn infant may be misleading; the cells may be coated with antibody and be inagglutinable by anti-Rh sera, thereby wrongly appearing as Rh-negative.

A great excess of nucleated red cells, if present, supports the diagnosis, but such excess is often absent.

DESIRABILITY OF ROUTINE RH TESTING DURING PREGNANCY

The routine Rh testing of antenatal patients should be made general as quickly as possible. In our series 58% of cases were the first affected pregnancies, where there could have been no previous obstetric history as a guide.

Apart from the importance of recognising iso-immunisation early from the point of view of the fœtus, the frequency of emergency transfusions in obstetric departments is in itself sufficient justification. In our series 9 cases were recognised through an incompatible transfusion, and 20 cases of erythroblastosis were probably attributable to a previous transfusion of Rh-positive blood.

Usually the blood is tested on the patient's first visit to the antenatal clinic. Where a woman is found to be Rh-negative but Rh-antibodies are not found, the blood should be tested again at about 34–35 weeks, since antibodies may not be apparent in the earlier months.

CONDUCT OF RECOGNISED CASES OF RH SENSITISATION

Explanation to Parents

When the iso-immunisation is recognised the mother and father should be interviewed and the problem explained to them. By this time they are usually worried either because they imagine that the extra blood samples have been taken because of some disease—e.g., syphilis—or because they have heard enough to make them realise that there is something seriously wrong and they cannot understand why. An explanation largely relieves their worry, increases their confidence in their medical advisers, and gains their coöperation.

Our routine has been a monthly examination of the serum up to 32 weeks followed by a weekly check from the 34th week, but on the whole the changes in antibody titre have been disappointing as a guide to prognosis. If a very great rise in the titre is found or the fœtal movements are much diminished, induction of labour must be considered. Induction of labour is usually undesirable before 36 weeks because of the dangers of prematurity. Occasionally one sees a series of titrations in which there is a rise in the titre followed by a pronounced fall, and in our experience this usually signifies that the fœtus is dead or dying.

Where the course of the pregnancy is uneventful, we advise surgical induction early in the 36th week, since the likelihood of death from erythroblastosis is steadily increasing after this time.

Treatment of Erythroblastosis Fœtalis

If the condition is anticipated through the presence of antibodies in the mother's blood ante partum, and is confirmed by a positive Coombs test on the infant's cord blood, the most satisfactory treatment is replacement transfusion by catheterisation of the umbilical vein. By using about a pint of blood about 80–90% of the infant's blood is removed and replaced by Rh-negative blood. We have had experience of this method for a year and feel that it has definite advantages over the older method.

If, however, as still often happens, the diagnosis is not made until the child is one or more days old, this technique is not available, and simple transfusion is indicated. We have no experience of replacement transfusion by the Wiener technique, in which blood is transfused into one vein while the infant's blood is being simultaneously removed from the radial artery. We feel definitely, with Parsons and Diamond, that the only effect of a simple transfusion is to compensate for the anæmia, and we consider that transfusion in a jaundiced child without anæmia is definitely contra-indicated. We have seen 3 children in other hospitals who died after this was done, in our opinion through plethora and cardiac failure.

The infant's hæmoglobin level, which should be estimated daily, is the basis on which transfusion requirements are determined.

If the jaundice appears on the first day of life and the hæmoglobin level is dropping rapidly, transfusion is required fairly quickly. When the onset is slower and the fall in the hæmoglobin less precipitous, we delay transfusion until the hæmoglobin is about 50%. This does not inconvenience the baby, and we think that the anæmia is a desirable stimulus to the infant's production of blood. From the practical point of view it permits the treatment of the infant with a single transfusion which will carry it through the period in which the whole of its initial supply of red cells is destroyed, and will usually maintain it until these have been replaced. As a rough guide, the average infant requires 35–40 ml. of stored blood to raise its hæmoglobin level by 10%. We therefore give about 250 ml. of compatible Rh-negative blood by a slow drip in 6–8 hours.

The older method of treatment with multiple small blood-transfusions does not give better results and offers far more technical difficulties.

Subsequent Treatment

The hæmoglobin should be checked regularly while the infant is in hospital and at gradually lengthening intervals after it has left. Most of these infants, being premature, tend to become anæmic, but this anæmia can be minimised by iron therapy during the first few months.

Apart from the administration of iron, the baby after discharge should be treated as a normal infant. Green pigmentation of the milk teeth occurs rarely in children who have been deeply jaundiced but is of no significance.

The infant should be watched for any abnormalities of movement, since these may herald the onset of the neurological complications of kernicterus later.

Breast-feeding.—In spite of the finding of antibodies in some specimens of milk, we feel that the dangers of bottle-feeding are greater than the questionable risk of absorbing antibodies from the milk. Cases where anæmia has apparently been maintained through absorption of antibodies are so few as to be in general disregarded.

TABLE II—OUTCOME OF 117 PREGNANCIES WHERE RH-ANTIBODIES WERE FOUND

Outcome of pregnancy	Total pregnancies	(*a*) Where pregnancy concerned is first affected	(*b*) Where there had previously been an affected pregnancy
Born alive	75	59	16
Survived neonatal period	52	41	11
Died during neonatal period	23	18	5
Not born alive ..	42	20	22
Hydrops fœtalis ..	12	4	8
Macerated stillbirths ..	21	13	8
Miscarriages	9	3	6
Totals	117	79	38

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TABLE III—PHENOTYPES OF 109 FATHERS OF ERYTHROBLASTOTIC CHILDREN

Apparently homozygous (containing two D genes = DD)		Apparently heterozygous (containing only one D gene = Dd)	
Rh_1Rh_1	38	Rh_1rh	23
Rh_1Rh_2	25	Rh_2rh	2
Rh_2Rh_2	3	..	..
Rh_1Rh_z	3	..	..
Totals ..	69	..	25

$Rh_z = 15$*

* These could not be divided into Rh_1rh and Rh_2Rh_z, since anti-z serum was not available at the time.

PROGNOSIS FOR THE UNBORN FŒTUS

Table II summarises the findings in 117 cases with Rh antibodies where adequate data were available.

First and Subsequent Affected Pregnancies.—The first important point is the difference between the first affected pregnancy and a pregnancy subsequent to the birth of an affected child. Of the first affected, 41 children from 79 pregnancies with antibodies survived (about 1 in 2), whereas in the subsequent affected pregnancies only 11 lived out of 38 (about 1 in 4). In general the disease becomes increasingly more severe in subsequent pregnancies, but this is by no means invariable. We have 3 cases where a stillborn child was followed by a live child in a later pregnancy, even though this later child was affected. When the father is heterozygous the chances are that half the later children will be Rh-negative and escape the disease altogether.

Pregnancy in which Disease was First Manifest.—In general the greater the number of normal pregnancies before the first affected one the better the prognosis. Thus there were only 24 live births from 38 first affected pregnancies when these were the patient's first or second pregnancy, whereas 30 infants out of 35 were born alive when the third or subsequent pregnancy was the first affected.

Intervals between Pregnancies.—It is often asked, "If I postpone my next pregnancy for a few years, will the prognosis be any better?" In our experience the answer is definitely "No." In our whole series there was no correlation between interval and prognosis. Once a woman has been sensitised she remains sensitised indefinitely. A subsequent pregnancy with an Rh-positive fœtus even after more than ten years immediately puts the antibody-producing mechanism into action. We have seen one blood donor who had an antibody titre of 1/256 thirty years after her last pregnancy.

Antibody Titre and Prognosis.—On the whole, though the value of antibody titres in prognosis is not great, the actual level of the antibody titre has some slight significance. High titres early in pregnancy—i.e., higher than 1 in 500—particularly of the blocking antibody, usually indicate a poor prognosis, but the contrary is not necessarily true. A consistently low titre may be followed by the birth of a seriously affected infant. In general a very pronounced fall in the antibody titre after the thirtieth week seems to imply a bad prognosis. A rise is, on the whole, less significant. The so-called "anamnestic response," where the titre has risen to more than four times its original level, has been met several times in our series in cases where the fœtus was Rh-negative and entirely unaffected.

Homo- and Hetero-zygous Fathers

The desirability of identifying the genotype of a father as homo- or hetero-zygous is obvious, since subsequent children of a homozygous father will all be Rh-positive and practically certainly affected with the disease, whereas with a heterozygous father 50% of subsequent children should be Rh-negative and unaffected.

The impossibility of identifying the genotypes with certainty by the sera at present available has already been referred to. A father can only be identified with certainty as heterozygous if a study of the blood-groups of all his offspring shows the presence of any Rh-negative children, or if he has an Rh-negative parent; for this reason family studies are desirable when possible.

We have tested serologically the phenotypes of 109 fathers. The distribution of the most probable genotype is shown in table III. In many the true genotype was confirmed by family studies. It is noteworthy that at least 74% were probably homozygous, whereas the normal proportion of Rh-positives who are homozygous should be 42.

PROGNOSIS FOR NEWBORN CHILD

Immediate Prognosis.—As can be seen from table II, if a child is born alive it has about a 2 to 1 chance of surviving the neonatal period, and there is no significant difference between first and subsequent affected pregnancies. The over-all mortality was 32% of the live births; but, since the cases occurred in many hospitals with very different ideas and skill in treatment, it should really be possible to reduce it below this figure, and in the cases dealt with at Lewisham Hospital the mortality was very much lower. Of the 23 deaths, 12 were due to kernicterus, very severe icterus gravis, or hydrops fœtalis, but in our opinion most of the remaining 11 children could have been saved: 2 died of sepsis, 2 through failure to transfuse because of technical difficulties, 4 through delay in making the diagnosis, and 3 from plethora through transfusion of infants with hæmoglobin values of 98%, 86%, and 98% with 200, 300, and 110 ml. of blood respectively. Of the surviving 52 infants, 41 were transfused. Of the 11 not transfused, in only 1 case was there gross anæmia, and in 5 cases the infant appeared normal though it was Rh-positive and the mother's serum contained Rh antibodies.

Long-term Prognosis.—Serious sequelæ of erythroblastosis as a result of kernicterus develop in a small proportion of patients and are rightly dreaded by the doctor. In our series we have followed up 34 children for more than a year, the two oldest being born in December, 1942. Of these cases serious neurological complications have developed in 4 (12%). In the worst case the child is apparently an ament. Others show various degrees of spasticity and mental retardation. The diagnosis of this condition in early infancy is very difficult. One child, who had severe jaundice but no notable neurological symptoms in the neonatal period, passed as an apparently normal baby for several months, and the diagnosis was not made with certainty till the child was over 6 months old. In some of these cases the apparent mental defect may possibly be due partly to a mechanical disability of expression, and it is hoped that some will be benefited by special re-education. The children who escape this tragedy are normal healthy children. If the nuclear damage does not develop, there is not in our experience any other abnormality or minor ill health; physically and mentally they form an average section of their age-group. They have had the usual childish ailments, and their reaction to infections was indistinguishable from that of a normal child. One child died of pneumonia after an operation for squint at the age of 1 year, and one has definite shortening of one leg following osteomyelitis due to blood-transfusion through the tibial marrow.

FURTHER READING

A list of references is out of place in a simplified summary such as this, but for those requiring further information the Medical Research Council *Memorandum*

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no. 19 on "The Rh Blood-groups," by Mollison, Mourant, and Race, provides the best up-to-date review of the subject. Further information on the clinical aspects is given in a paper by Parsons (*Lancet*, 1947, i, 815), and on the pathology of the condition in Potter's book "Rh" (Year Book Publishers, Chicago, 1947).

Our thanks are due to the clinicians and pathologists, too numerous to mention individually, who have allowed us to investigate their cases and sent us sera; Dr. R. R. Race and Dr. A. E. Mourant for supplies of special sera and for coöperation in many other ways; and the technicians without whom this work would have been impossible—particularly Miss C. R. Spittle, Miss B. J. Edwards, Mr. J. E. S. Greenstreet, and Mr. R. J. Buttimer.

INTESTINAL LIPODYSTROPHY

(WHIPPLE'S DISEASE)

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"A HITHERTO undescribed disease characterised anatomically by deposits of fat and fatty-acid crystals in the intestinal and mesenteric tissues." Such was Whipple's description, in 1907, of a malady which caused the death of a medical missionary aged 36. Since then, less than 25 reports have appeared dealing with the same or a similar condition. As the number of theories, past and present, suggests, the cause has not yet been found.

In this country only 2 cases have been published (Glynn and Rosenheim 1938, Vaux 1943). Cases elsewhere have been reviewed by Blumgart (1923), Fleischmann (1930), Jarcho (1936), Hill (1937), Korsch (1938), Boeck (1938), Reinhart and Wilson (1939), Amsterdam and Grayzel (1945), Fitzgerald and Kinney (1945), Oliver-Pascual et al. (1947), Sailer and McGann (1942), Apperly and Copley (1943), and Rosen and Rosen (1947). The last three papers contain helpful summaries on the subject.

Pemberton et al. (1947) have described 3 cases diagnosed as intestinal lipodystrophy by mesenteric biopsies during life. The equivocal picture in these cases may, as they point out, be due to the disease being in an early stage. Further reports will be awaited with interest. Intestinal lipodystrophy may be less rare than figures suggest and masquerade under such diagnoses as atypical Addison's disease, various mesenteric lymphadenopathies, nutritional deficiency states, sprue syndrome, and carcinoma of the pancreas. It is difficult to see how a case could be overlooked at necropsy, but it is likely that some patients with intestinal lipodystrophy are sent home to die and do not come to necropsy.

Most patients have been middle-aged men, and the duration of symptoms before death has usually been 1–5 years though sometimes much longer. Stabbing central abdominal or epigastric pain has been common at the outset. Fever is not always present, and bleeding per rectum, when sought for, has been more often found than not. A history of "arthritis" affecting more than one joint has been given by some patients. Increasing lassitude, loss of weight, diarrhœa, and steatorrhœa herald the terminal phase. Brown pigmentation of skin and oral mucosa and hypotension have often suggested Addison's disease. Anæmia, achlorhydria, signs of vitamin deficiencies, hypoproteinæmia, ascites, and œdema may appear before the end.

CASE-RECORD

A man, aged 44, served in the Army from 1941 to 1945 but did not go abroad. After his demobilisation in October, 1945, his wife dissuaded him from returning to his pre-war work as a Covent Garden porter, and he took up factory employment. By August, 1946, when his illness began, he had found a job which suited him. His first symptom was central abdominal colicky pain, accompanied by the passage of blood per rectum. He drew his wife's attention to the blood in the lavatory pan, and she urged him to see a doctor. Blood per rectum persisted for at least some days. He attended Central Middlesex Hospital in October, 1946, when a barium meal showed nothing abnormal and a diet was recommended. His weight was then 8 st. 9 lb. in his clothes. In November, 1946, his diarrhœa was severe, and on Jan. 9, 1947, he attended another hospital because of increasing malaise. He was examined with negative results, his blood-pressure was 130/90 mm. Hg and a radiogram of the chest was clear; some carious teeth were extracted. He returned and was admitted to Central Middlesex Hospital in March, 1947. His stools were frequent, watery, and grey; no blood was noted in them. He weighed 7 st. in his clothes at this time.

The past history was not clear, but it appeared that he had had dyspepsia for a fortnight in 1942, and had reported sick on several occasions in the Army with "rheumatism, which, according to his widow, amounted to pain and tenderness of the legs, mainly the calves. From 1943 onwards he had often been troubled with painless pitting œdema of the ankles; he may have had thrombophlebitis. In 1941 he had noted that the vision in his right eye was blurred, and within a day or two the eye had become blind. Right retrobulbar neuritis was diagnosed. He never recovered the sight in this eye, and right optic atrophy was discovered when he was examined in 1946. His habits were always temperate.

He was the eleventh of 13 children, boy and girl twins being younger than he. His parents were costers, out most of the day, and the last 3 children were brought up by an elder sister, whom the patient never liked. He was barely literate, whereas the twins were much better educated, and the girl was inclined to "pull his leg." He grew up a steady quiet sensitive fellow given to fits of brooding. His family were astonished when he married. His wife noted a great change in his manner between October, 1945, and August, 1946. He no longer played with the children, who appeared to irritate him. He became withdrawn and would not speak except when alone with his wife, when he would become very talkative. He was apparently impotent after his release from the Army. On one occasion when he attended hospital elsewhere he complained of this symptom and of blood per rectum. Unfortunately the students chose that moment to laugh at something else, but he was convinced that they were laughing at him, and, deeply hurt, he told his wife he would not return there. Much of the information above was gained from his widow. The patient's own account was incomplete and typical of his reticence.

On admission (August, 1947) the patient was afebrile but extremely emaciated with a generalised brown nonscaling pigmentation of the face, lips, and mucosa of the mouth. His skin was dry and inelastic. There was no icterus. The tongue was normal, but there was some angular stomatitis. Blood-pressure 110/70 mm. Hg. The abdomen was distended and hyper-resonant; there was no free fluid clinically. The edge of the liver was palpable, but no mass was felt. No abnormality was detected in the chest or central nervous system.

Investigations.—A barium meal showed a coarse irregular mucosal pattern in the duodenum and jejunum. Radiograms of the chest and abdomen (with barium enema) were normal. Sigmoidoscopy was normal. Many microscopical examinations of fæces revealed only once some pus cells and once a few undigested meat-fibres and starch granules. Fæces culture and occult-blood tests were negative. A blood-count showed red cells 3,900,000 per c.mm., Hb 52%, colour-index 0·67, white cells 7700 per c.mm. (polymorphs 73%, lymphocytes 25%, monocytes 2%). Urinary chlorides were usually low—on one occasion 0·7 mg. per litre. Serum-sodium was 324 mg., potassium 24 mg., and calcium 8·1 mg., per ml. A Robinson-Power-Kepler test was normal. There was a histamine-fast achlorhydria, and a flat glucose-tolerance curve was obtained. Fat-balance showed that 78·5% of ingested fat was being absorbed; the normal is 90% or more (Cooke et al. 1946).

Treatment.—The following measures were tried without success: (1) high-protein low-fat diet, with added vitamins;

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(2) 'Doca' 10 mg. daily, and subsequently suprarenal cortical extract in addition; (3) folic acid 20 mg. daily for two or three weeks; (4) crude liver extract. Various steps were taken to control the diarrhœa, with little success. Sodium chloride capsules and saline infusions helped temporarily, but the blood-pressure continued to fall, the systolic pressure fluctuating between 90 and 100 mm. Hg.

The patient discharged himself from hospital on July 1, 1947, and was readmitted on the 7th with increased weakness and diarrhœa. He refused further investigations or intravenous therapy. His weight was then 6 st. 2 lb., and he steadily deteriorated until his death on Aug. 6, 1947.

Necropsy Findings.—There were many peritoneal adhesions and "sugar icing" of liver and spleen. The liver weighed 1150 g. and was somewhat œdematous. The spleen weighed 130 g. The first 2½ ft. of the jejunum was normal, the rest of the small intestine being atrophic and plum-coloured, except for 15 cm. in the middle of the ileum and the terminal 28 cm., which were pigmented and almost black. The lymphoid tissue in the ileum was hypertrophied, and small whitish-yellow deposits were present in the intestinal wall. The mesentery contained many firm glands of the size and shape of almonds, their cut surfaces being pale and somewhat cystic in appearance. There was no pigmentation beyond the ileocæcal valve, and the large bowel was normal.

Microscopy.—The pancreas was normal. The suprarenal glands showed "pyknosis" (fuchsinophilia) of the cortical cells, with depletion of lipoid. The appearances were similar to those in starvation and deficiency states (W. Pagel, personal communication). The mesenteric-gland sinuses were grossly dilated with fat. Foamy macrophages predominated, and giant cells were present but scanty. There was some fibroblastic activity. The small gut showed the characteristic club-shaped villi stuffed with intracellular and extracellular fat (figs. 1 and 2). There was evidence of low-grade inflammatory reaction, and eosinophils were rather numerous.

DISCUSSION

The present case does not differ materially from those previously reported. Abdominal pain was the presenting symptom and did not persist. Pigmentation was well-marked, and, together with hypotension, this suggested Addison's disease, but biochemical investigations, the normal Robinson-Power-Kepler test (Robinson et al. 1941), and a lack of response to specific therapy contra-indicated suprarenal insufficiency.

Skin pigmentation of a type similar to that in Addison's disease is often associated with idiopathic steatorrhœa (Thaysen 1932, 1935, Snell 1939, Prunty and Macoun 1943), sprue, and chronic diarrhœas (Jeghers 1944). It

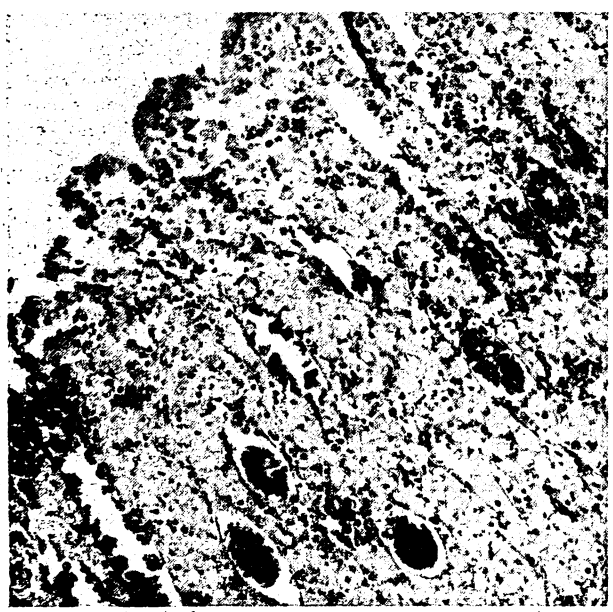

Fig. 1—Section of intestine showing club-shaped villi full of foam cells. (× 50.)

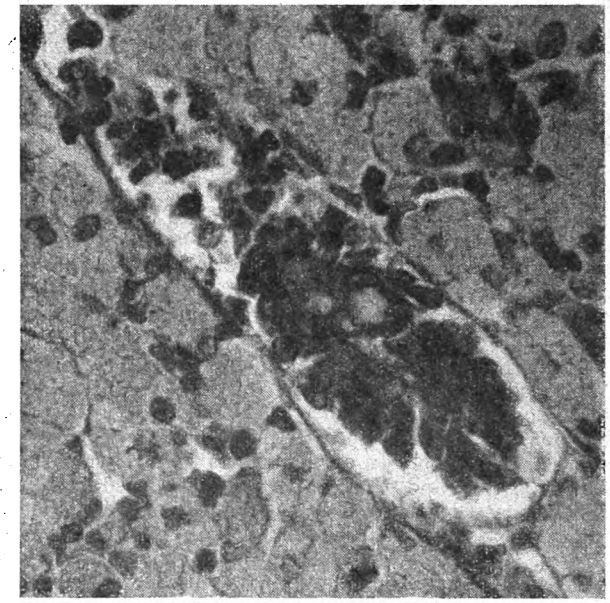

Fig. 2—Same as fig. 1. (× 200.)

has been suggested that the colour is not so deep as in suprarenal insufficiency, and that the mucosæ tend to escape (Thaysen 1932). Pigmentation was present in 12 out of 34 steatorrhœa cases (Thaysen 1932) and in 7 out of a further 10 (Thaysen 1935). Snell (1939) found it in 22 out of 32 patients with non-tropical sprue. Hypotension has been usual (Thaysen 1932, Snell 1939, Prunty and Macoun 1943, Black 1946). Excessive loss of sodium is common to all these disorders, and, whereas in Addison's disease the loss is renal in origin, in diarrhœa there is an impaired reabsorption of upper-bowel secretions (Black 1946), which contain a predominance of sodium over chloride (Gamble et al. 1945). This probably represents part of the truth but not all of it. A study of the published reports on Whipple's disease shows that in no case was pigmentation not associated with bowel looseness; in some it was of long standing, in others it was not. Locket (1945) described a case with steatorrhœa, hypotension, pigmentation, and melanuria. Perhaps melanuria is commoner in cases of this sort than has hitherto been recognised, and this is suggested by the work of Haden and Orr (1923, 1924), whose interest was aroused by finding melanuria in a case with high intestinal obstruction. They later collected several similar cases with hypochloræmia from vomiting due to intestinal obstruction and after gastro-enterostomy. Melanuria was present in all, and cleared as the urinary sodium-chloride level rose on treatment with saline.

Some workers (Wilkinson and Ashford 1936, Sodeman 1939, Rothman 1942) have held that the pigmentation in Addison's disease is related to low ascorbic-acid levels. (Experimentally the presence of ascorbic acid tends to inhibit the dopa reaction.) Claims have been made for reduction in pigmentation with large doses of vitamin C (Snell 1939). Lea (1945) has shown in vitro that a low concentration of sodium chloride, by increasing the destruction of ascorbic acid by oxidation, indirectly encourages the formation of melanin from tyrosin.

A deficiency of adrenocortical secretion has often been suspected in the steatorrhœas for the reasons already given and consequent on the work of Verzár and McDougall (1936). Nevertheless, treatment with desoxycortone and cortical extracts has been unconvincing, and Prunty and Macoun (1943) and Black (1946) have brought forward biochemical evidence against

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any suprarenal insufficiency in these conditions. It is not surprising in view of its patholgoy that Whipple's disease should also present features of "addisonism," and that patients with the condition should have received treatment for Addison's disease without benefit (Glynn and Rosenheim 1938, Sailer and McGann 1942), though it has probably been given with more hope than conviction, as in the present case.

In the present case a fat-balance estimation, by the method of Cooke et al. (1946), showed a slight defect in the absorption of ingested fat. The postabsorptive systemic lipæmia has yet to be estimated in Whipple's disease, but Frazer's work (Frazer et al. 1944, Frazer and Sammons 1945, Frazer 1946) suggests that it is most likely to be low, as in sprue.

Numerous theories have been put forward to explain Whipple's disease, and some of them concerning a breakdown in the normal physiology of absorption depend on Verzár's lipolytic hypothesis. Verzár considered that lipolysis of neutral fat was complete in the intestine, and that it was all absorbed as fatty acid to be resynthesised in the intestinal cell by phosphorylation under the possible control of the suprarenal cortex. Frazer's work has shown that there are weaknesses in this hypothesis, and he has put forward instead the partition theory, which assumes incomplete lipolysis under normal conditions and, with adequate emulsification, the absorption of much neutral fat in particulate form. He has shown that fatty acids pass via the portal vein to the liver, and that triglyceride moves to the fat depots via the blood-stream. The mobilisation and carriage from the intestinal cell involve factors not yet understood, but there is evidence that choline and phospholipid may play a part. Abnormality of this mechanism has to be considered as a cause of Whipple's disease.

Fatty tissue from previously reported cases has been found on analysis to contain mainly neutral fat, fatty acids and cholesterol representing only a small part (Whipple 1907, Sailer and McGann 1942, Apperly and Copley 1943, Rosen and Rosen 1947).

There is no evidence that the condition represents the intestinal form of one of the known lipoidoses. Where search has been made the thoracic duct and main lymph channels have been patent; and in conditions of lymphadenopathy described by Fairley and Mackie (1937), causing obstructive steatorrhœa, fat had not accumulated in the villi, mesentery, or gland sinuses. However, a partial obstruction, low-grade and sclerosing, is perhaps not so unlikely. With this in mind reference must be made to the lipophagic granulomas produced experimentally in animals by Paterson (1938) and Hass (1938) and clinically seen in such conditions as lipoid pneumonia and paraffinoma in man. If small quantities of some alien substance, fat or oil, were taken up by the intestinal cells, sufficient reaction and scarring might develop to impede the removal of fat ingested subsequently, the accumulation of which might obscure the original histology. Alternatively a granulomatous condition might develop as a response to normal fat escaping into the tissues from ruptured lacteals during absorption. Evidence suggests that the histological response would vary with the melting-point and degree of saturation of the fat (Paterson 1938, Hass 1938). Unsaturated fatty acids have been observed to cause the most acute cellular reaction, with foam cells prominent and intracellular fat predominating over extracellular fat. On the other hand, saturated neutral fat produces the picture of a foreign-body reaction, with much extracellular fat, many giant cells, and fewer foamy macrophages. The histological reports and photomicrographs of previously reported cases of Whipple's disease show variations of this type. In some instances giant cells have been very numerous, in others they have been scanty. If there is a partial obstruction of the flow of fat to the thoracic duct, the likely site would be at the efferent side of the mesenteric lymph-gland, and such a condition could predispose to lacteal engorgement and possible rupture. Subsequent lipophagic granulomatous response might well lead in the end to a more complete obstruction.

If in place of fat-filled lymphatics in Whipple's disease lymphœdema is substituted, the histology is not very unlike that found in Crohn's disease. The differences there are may depend more on the part of the gut involved than on fundamental differences of ætiology. The giant-cell inclusions often described in regional ileitis (Moschcowitz and Wilensky 1927, Binney 1935, Barbour and Stokes 1936, Meyer and Rosi 1936) have been thought by many to represent food remnants (perhaps lipoid) caught up in a highly developed and avid lymphatic system.

Regional jejuno-ileitis has been described by Crohn and Yunich (1941) as more diffuse, less often stenosing, and less liable to tumour and fistula formation than terminal ileitis. But segmental cicatrising jejunitis has often been reported, and has occasionally developed in long-standing cases of cœliac disease and idiopathic steatorrhœa (F. Avery Jones, unpublished). It has not yet been observed in Whipple's disease. Nevertheless, we suggest that intestinal lipodystrophy may represent a variant, or a resultant (or terminal), phase of a "jejunitis," such a "jejunitis" being possibly a non-specific inflammation of a hyperæmic œdematous mucosa with parallels in colitis, ileocolitis, and "gastritis." The finding of blood in the stools at the outset of the disease supports this view.

The matter might be clarified if tissue from cases of regional jejunitis were carefully examined for any evidence, however early, of Whipple's disease. The age-incidence is some 15 years higher than the average in regional ileitis, but this is not unreasonable if scarring of the mesenteric glands is a necessary preliminary. The present patient's personality coincided broadly with that found in other intestinal dysfunctions recognised as psychosomatic, and is in accord with Paulley's (1948, 1949) findings in a limited series of cases of regional ileitis, and a few cases of cœliac disease and idiopathic steatorrhœa.

Further exhaustive study of Whipple's disease may shed light on other more common but still obscure forms of steatorrhœa.

SUMMARY

A fatal case of Whipple's disease is described.

The main findings of earlier workers are summarised.

Pigmentation in Whipple's disease is discussed in its relation to Addison's disease and conditions where there is increased loss of sodium.

It is suggested that Whipple's disease may possibly originate in a primary non-specific "jejunitis."

The patient's personality coincided broadly with that found in regional ileitis and some other intestinal disorders believed to be psychosomatic.

We wish to thank Dr. W. Pagel for the histological reports and photomicrographs.

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ACUTE PHENOBARBITONE POISONING

TREATMENT WITH PICROTOXIN

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As a pleasant and convenient chemical means of self-destruction barbiturates are becoming ever more popular. In the United States they cause over 400 deaths by suicide annually, being exceeded only by coal-gas poisoning, and in their country of origin, Germany, they account for 6% of all cases of poisoning. In England they are not so readily obtainable, owing to the safeguards of Schedule IV, but in the last decade their invaluable sedative and hypnotic properties have made the barbiturates articles of everyday use. Large quantities may be obtained over a period by repeated presentation of a prescription or by amassing supplies received in the hospital outpatient department ("Rep. tabs").

Gillespie (1934) was able to collect only 157 reported cases of suicide from barbiturates up to 1932, and he therefore decried their importance as suicidal agents. Scarlett and Macnab (1935) found 408 cases, of which 60% had occurred in 1933–34. In 1925–32 there were 164 deaths (suicidal and accidental) in England and Wales from barbiturate poisoning, of which 77 were ascribed to 'Veronal' (barbitone), 34 to 'Medinal' (sodium barbitone), 23 to 'Dial' (diallyl barbituric acid), and 10 to 'Luminal' (phenobarbitone). During the subsequent seven years there were 376 deaths, which are analysed in the accompanying table, compiled from the Registrar-General's statistical reviews.

Deaths from coal gas and aspirin increased absolutely and relatively to the total deaths from poisoning; the number of barbiturate deaths rose until 1935 and then fell for three years after the establishment of the Poisons Rules, 1935. Later, possibly owing to wider use and more lax interpretation of these rules, deaths from barbiturate poisoning steadily increased. Of all suicides from solid and liquid poisons, the proportion due to barbiturates rose from 5·5 to 8·5%, and barbiturates were responsible in 1939 for over 20% of "accidental" deaths from non-gaseous poisons. The figures for suicidal and accidental deaths from barbiturate poisoning are best considered together, since the distinction between accident and suicide cannot always be accurately made; there is probably suicidal intent in most cases, but a few may result from true barbiturate automatism (see below).

The choice of barbiturate by suicides varies, as would be expected, with its clinical vogue; thus barbitone was responsible for 11 deaths in 1933, and for only 6 in 1939. Between 1925 and 1932 only 6·6% of barbiturate deaths were caused by phenobarbitone, whereas by 1939 the proportion had risen to 36%; actually it was probably nearer 50%, since in a dozen cases the barbiturate involved was not specified. Formerly deaths from sodium barbitone and barbitone each exceeded those from phenobarbitone, but since 1935 phenobarbitone has caused more deaths than the other two drugs together.

Figures for the war years are not yet complete and comprise only the violent deaths among civilians; but, if the available statistics for 1933–46 are plotted as a graph (see figure), definite trends become evident. Deaths from barbiturate poisoning have greatly increased. Thus, in 1946, 139 persons died from this cause—an increase of 280% on the 1933 figures. In 1947 there was probably an even larger number of barbiturate deaths. The proportion of deaths from barbiturates to all deaths from poisoning has risen steadily from 1·5 to 6·3%, while the annual number of deaths from all forms of poisoning has fallen by 20%. Of the barbiturates, phenobarbitone is now much the most frequently used in suicide, doubtless because of its very extensive use as a sedative—to slow the tempo of modern life. The name has become a household word and the lay public is conscious of its potentialities as a poison, thanks to the publicity given by the B.B.C. whenever a few tablets are mislaid.

TOXICOLOGY

The average lethal dose of a barbiturate is 15–30 times its pharmacopœial dose, but there is a wide variation in individual response; especially unfavourable are increasing age, respiratory infection, cardiovascular disease, and impairment of hepatic or renal function. Mutch (1934) gives the ratio of the minimal lethal dose to the therapeutic dose for phenobarbitone as 1·3, for barbitone as 1·6, for 'Soneryl' (butobarbital) and 'Nembutal' (sodium ethylbutylbarbituric acid) as 2·4, and for 'Evipan' (hexobarbitone) as 5; thus, of these five common barbiturates, phenobarbitone has the lowest margin of safety or "therapeutic breadth," and it is not safe in full hypnotic dosage. The average lethal dose is about gr. 60 (3·8 g.), but death has been reported from gr. 26 (1·7 g.) (Sollmann 1942), and recovery has taken place spontaneously from gr. 90 (5·8 g.). A single dose acts for 18–24 hours, and the effect may be cumulative, for elimination is slow and occurs mainly by oxidation in the liver, only 10–40% being recoverable from the urine (Fretwurst et al. 1930). No real tolerance is developed, even by habitual users, though these may develop the confusional state known as barbiturate automatism, in which they may take large doses repeatedly. Phenobarbitone has a strongly depressing action on the emotions; so it should not be prescribed for a potential suicide. Hypersensitivity to the drug is rare. Alcohol appears to have a synergistic effect.

In acute phenobarbitone poisoning there is a brief period of headache with increasing drowsiness, confusion, ataxia, and sometimes twitching, passing into sleep and finally coma. Breathing becomes slow and shallow, pulmonary œdema supervenes with remarkable rapidity, and pneumonia often follows. The body temperature falls at first, and then rises. Muscle tone is diminished, reflexes are sluggish, and the pupils are small and perhaps unequal. A fall in blood-pressure leads to oliguria, and the urine may contain albumin, sugar, and hæmatoporphyrin. The patient dies from medullary depression, cerebral œdema, or pulmonary infection, but recovery

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may occur even after 6–8 days in coma. At necropsy there are widespread degenerative changes in the central nervous system, and fatty degeneration in the liver, kidneys, and capillaries.

TREATMENT

Treatment includes measures to aid the elimination of the drug, the relief of symptoms arising from medullary depression and coma, and stimulation with a pharmacological antidote.

The stomach should be washed out at once with sodium bicarbonate or potassium permanganate solution or a suspension of charcoal, 2 oz. of magnesium sulphate being left in the stomach. Fluids should be given liberally, but in the presence of pulmonary or cerebral œdema the intravenous route is best avoided. Elimination by forced diuresis with ammonium chloride or a mercurial diuretic has been recommended. Removal of cerebrospinal fluid was advocated by Willcox (1934); it is doubtful if much phenobarbitone can be removed by lumbar puncture, for the concentration of the drug in the cerebrospinal fluid is considerably less than in the blood, but the procedure is of value when cerebral œdema is present.

A clear airway should be ensured by suction, and atropine given to reduce bronchial secretion; the patient should lie on his face with the foot of the bed raised, to reduce the risk of his aspirating his secretions, and he should be frequently turned and penicillin given to prevent pneumonia or lung abscess. Respiration may need stimulation with oxygen and carbon dioxide, and an "iron lung" should be available.

Picrotoxin

The safest and most effective analeptic, with the most truly physiological antagonism to barbiturates, is picrotoxin. This is a crystalline non-alkaloidal substance obtained from Levant nuts (*Cocculus indicus*) and is a powerful convulsant, acting chiefly on the respiratory and other medullary centres. Its use in morphine poisoning was suggested in 1847, but it remained something of a pharmacological curiosity until Maloney et al. (1931) and Maloney and Tatum (1932) demonstrated effective picrotoxin-barbiturate antagonism in animal experiments. It is, however, difficult to demonstrate directly that picrotoxin has saved human lives, because the fatality of untreated cases varies widely and overlaps with that of treated cases. The Council on Pharmacy and Chemistry of the American Medical Association (1939) pointed out that even in convulsive doses picrotoxin may not establish consciousness directly. The consensus of clinical opinion, backed by the controlled experiments of Maloney et al. (1931), Maloney and Tatum (1932), and Bleckwenn et al. (1940), appears to be that picrotoxin is of value in hastening recovery, prolonging life, and to a limited extent in decreasing the fatality-rate. By assisting in the maintenance of respiration and circulation it allows time for elimination of the barbiturate to proceed until consciousness returns.

FATAL POISONING IN ENGLAND AND WALES

Year	Total of suicides	Deaths from poisoning								
		Suicidal or accidental	Solid or liquid poisons	Barbiturates	Phenobarbitone	Soluble barbitone	Barbitone	Other and unspecified barbiturates	Aspirin	Carbon monoxide
1933	5654	Sui.	816	26	5	8	5	8	9	1732
		Acc.	106	25	4	7	6	8	7	136
		Both	922	51	9	15	11	16	16	1868
1934	5550	Sui.	749	30	6	11	4	9	10	1863
		Acc.	93	16	3	3	4	6	11	141
		Both	842	46	9	14	8	15	21	2004
1935	5223	Sui.	657	34	4	7	8	15	36	1779
		Acc.	91	29	11	6	3	9	7	183
		Both	748	63	15	13	11	24	43	1962
1936	5079	Sui.	562	33	10	10	3	8	17	1771
		Acc.	95	17	7	2	1	7	7	229
		Both	657	50	17	12	4	15	24	2000
1937	5165	Sui.	580	27	9	6	3	9	41	1770
		Acc.	98	19	6	4	1	10	10	211
		Both	678	48	15	10	4	19	51	1981
1938	5316	Sui.	591	38	15	7	5	11	43	1990
		Acc.	92	15	8	2	0	5	8	243
		Both	683	53	23	9	5	16	51	2233
1939	5054	Sui.	519	47	13	8	5	11	36	1981
		Acc.	72	18	5	4	1	3	7	175
		Both	591	65	18	12	6	14	43	2156
Totals	37,041	All poisonings	5121	376	106	85	49	119	249	14,204

Comparison of two series of cases, one treated without and the other with picrotoxin, lends support to this impression. Leschke (1933) quotes 10 cases of phenobarbitone poisoning between 1925 and 1928 treated with injections of camphorated oil; the average fatal dose was gr. 60 (3·8 g.) and the maximum survived gr. 90 (5·8 g.), this patient lying unconscious for seven days. In Hambourger's (1940) series of cases treated with picrotoxin the amount of phenobarbitone taken in fatal cases averaged gr. 143 (9·3 g.), and the largest dose survived was gr. 135 (8·7 g.). Some of Hambourger's cases received sulphonamides, which reduced the incidence of pulmonary complications, but the inference, nevertheless, is that picrotoxin can be a life-saving drug.

Picrotoxin does not appear to have any lasting ill effects even in high dosage (Richards and Menaker 1942). It should be given continuously or repeatedly in small doses, because it is rapidly removed from the blood and a steady concentration is needed to counteract the continuous and protracted action of slow-acting barbiturates. It should be pushed just to the point of spontaneous movement, but convulsions must be avoided because of the resultant postconvulsive depression, and thiopentone should therefore be at hand to counteract the effect of inadvertent overdosage.

Very large total doses of picrotoxin may be necessary; in successful cases doses have varied from a few milligrammes to 1944 mg. (Richards and Menaker 1942). Rovenstine (1938) gave doses ranging from 60 to 1820 mg. in his successful cases, recovery occurring in patients who had taken gr. 70–90 (4·5–5·8 g.) of phenobarbitone. Another patient, however, died on the eighth day after taking gr. 500 (32·4 g.) of sodium barbitone, in spite of receiving picrotoxin 2134 mg.; and Richards and Menaker (1942) report a case where the patient died on the fifth day of pneumonia after receiving 2296 mg. of picrotoxin. In such cases the failure of picrotoxin is probably attributable to brain damage from prolonged anoxia.

Metrazol and 'Coriamyrtin' have also been used as stimulants. Bleckwenn et al. (1940) found experimentally that coriamyrtin was the most powerful stimulant, followed by picrotoxin and metrazol, but that it was not safe, because it often led to convulsions. Picrotoxin had a longer action than metrazol, but metrazol was a more powerful stimulant of the higher centres, and might be useful in the later stages of treatment when the medullary and subcortical centres had been "denarcotised" with picrotoxin.

CASE-RECORD

A man of 25, weighing 11 st. 10 lb. (74·5 kg.) and previously healthy, was found unconscious in bed on the morning of

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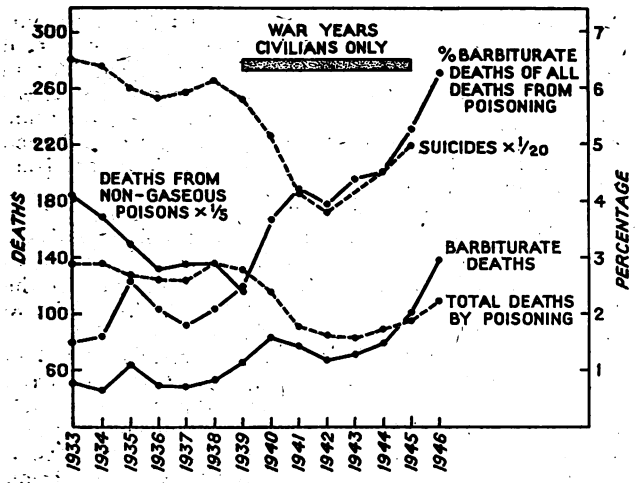

Relation of number of deaths from barbiturate poisoning to other forms of poisoning and to total number of suicides in 1933–46 (amended from *Chemist and Druggist*, March 27, 1948).

Dec. 5. On admission to hospital he was deeply comatose, with no response to pain stimuli. Muscles were flaccid, superficial and deep reflexes absent, and pupils slightly dilated, equal, and fixed. The fundi showed large colobomata of both maculæ. Temperature was 99°F, pulse small and thin; blood-pressure 90/60 mm. Hg. Respirations were shallow and bubbly, 16 per min. The skin was dry and cyanotic, tongue furred, but breath free from smell, and the pharynx full of thick sticky mucus. Râles were audible throughout both lungs. The urine did not contain albumin or glucose but gave a positive Gerhardt test.

A provisional diagnosis of narcotic, probably barbiturate, poisoning was made, and nikethamide 5 ml. was injected intravenously, without response. No history of drug-taking could be obtained from the parents; so, while the stomach was being washed out with sodium bicarbonate, a visit was made to his house. A pill-box was found hidden in his bedroom, and the chemist whose name appeared on it informed me that the box had contained gr. 60 of phenobarbitone sodium dispensed the previous day. Two prescriptions were also discovered, one for gr. 30 and the other for gr. 60 of sodium phenobarbitone monthly, and both had been stamped on Dec. 4. It thus appeared that the patient had taken at least gr. 90 of phenobarbitone.

The stomach wash was returned clear. He was given 5 ml. of 0·3% picrotoxin solution—i.e., 15 mg.—intravenously, with momentary deepening of respiration and rise of blood-pressure to 120/70 mm. Hg, but no movement resulted. At 1.15 P.M. lumbar puncture gave a clear fluid under increased tension (not measured) and 30 ml. was removed. The fluid showed no serological or cytological abnormality, but by mischance was not examined for barbiturate. Subcutaneous injections of 2 ml. of picrotoxin (6 mg.) were then given every 15 min.; the pharynx was kept clear by swabbing and suction, and an airway was inserted. Atropine gr. $^1/_{75}$ and penicillin 100,000 units were given b.d., and the patient was turned frequently, since fine crepitations were now audible over the lungs. Copious fluids and a high-calorie diet were given by stomach-tube.

On the evening of Dec. 5 he was still deeply unconscious, and his temperature had risen to 102°F. Cyanosis had been superseded by flushing of the skin and sweating. The pupils were small and reacted very slightly and sluggishly to light. Blood-pressure was 95/65 mm. Hg. The urine was pinkish and reduced Benedict's reagent. During the night he remained in deep coma but had short periods of restlessness and excitement after the picrotoxin injections.

Next morning, Dec. 6, he still could not be roused. His pupils reacted well to light, the deep reflexes had returned but were sluggish, and the plantar responses were flexor. An intravenous injection of picrotoxin 5 ml. produced tonic spasms with twitching of the face and movements of the arms, at intervals of a few seconds for about 5 min. He would not tolerate the stomach-tube, and fluids had to be given by rectal drip. Lumbar puncture was repeated, but the fluid was under low pressure and only 5 ml. was removed. This specimen was normal, and no barbiturate could be demonstrated in it. During the evening he became excitable and violent, with one tonic-clonic spasm. Picrotoxin was discontinued for 3 hours, and after $1^1/_2$ hours he relapsed into deep sleep. When picrotoxin was restarted, he became sufficiently conscious to recognise his mother, but then became violent and had to be quietened with nitrous oxide. During Dec. 5 and 6 there was oliguria, with the excretion of only a few ounces of urine.

On Dec. 7 he was rousable by strong stimulation. Temperature 99°F, chest clear. Picrotoxin 2 ml. was given every 20 min. That evening he was less drowsy and would respond with effort when questioned, but his speech was thick and slurred. There was ataxia with a fine tremor of the hands. Picrotoxin was continued half-hourly during the night. Next day he could be roused more easily, saying he felt very drunk. During the preceding 24 hours he had a large diuresis with a urinary output of 273 oz. on a fluid intake of 116 oz. Blood-pressure was 125/85 mm. Hg. Atropine and penicillin were finally stopped, but picrotoxin was continued because of the possibility of relapse.

On the 9th he was sleepy but readily rousable. He improved rapidly, and picrotoxin was stopped at 2 P.M. after a total of 1650 mg. had been given. Urinary excretion remained greater than fluid intake for several days.

He made a rapid and uneventful recovery thereafter, and before his discharge told the following story. In January he had, unknown to his parents, complained to a doctor of restless nights and frequent nocturnal emissions. He was given a prescription for phenobarbitone sodium gr. 1 o.n., to be repeated monthly; this he mislaid and so obtained a second prescription, made out for gr. 2 o.n. He later found the first prescription and had used one or other occasionally to obtain a good night's sleep. He had always been handicapped by partial blindness owing to congenital colobomata of both retinæ, and recently he had become depressed at the loss of a series of teaching appointments because of his bad sight. Feeling that he was a failure he decided to commit suicide. On Dec. 4 he obtained a month's supply of phenobarbitone on each prescription, and on retiring to bed at 10.30 took the gr. 90 together with about twenty-five more gr. 1 tablets, making a total of gr. 115 (7·5 g.). He intended also to take the whole of a bottle of fifty aspirins but eventually swallowed only some thirty gr. 5 tablets, since he found them more unpleasant than phenobarbitone. He quickly fell asleep, and the next he remembered was fighting to get out of bed and turn on the light. He thought this was a nightmare, but in fact on the night of Dec. 6, while under picrotoxin, he became violent and tried to get out of bed to the light switch (which was turned on). It thus appears that the first partial return of consciousness took place within 36 hours of the start of treatment and was associated with subconvulsive doses of picrotoxin.

COMMENT

This man survived without ill effects after an amount of phenobarbitone which, before the advent of picrotoxin, would have been considered about twice the average fatal dose; within 40 hours the first glimmerings of consciousness had returned, and within 3 days he was completely rousable. The maximal recorded dose survived without picrotoxin treatment is gr. 90, the patient remaining unconscious for 8 days. Our patient had also taken gr. 150 (9·7 g.) of aspirin, which would have an additional depressant action on the respiratory centre, though in a person of normal sensitivity it would constitute only a third or less of the average fatal dose. It was not appreciated that he had taken aspirin, and the positive Gerhardt's test in the urine was wrongly attributed to mild ketosis. There was no obvious acidosis and no sign of aspirin intolerance.

The considerable degree of pulmonary œdema which rapidly supervened is a constant and noteworthy feature of barbiturate poisoning, and has been ascribed to a direct toxic action of the drug on the capillaries of the lung (Jacobi 1923). No pulmonary complications developed, however—compare cases described by Misir (1946) and Richards and Menaker (1942).

Gastric lavage should never be omitted, even if a considerable time has elapsed since ingestion of the drug, for the rate of absorption is variable and in the presence

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of chronic gastritis may be greatly prolonged. In the stomach of a chronic alcoholic who died 15 hours after taking sixty gr. 5 tablets of sodium barbitone, I once found fifteen tablets still embedded in mucus and showing only slight decomposition.

A total of 1650 mg. of picrotoxin was given in 5 days; though consciousness had returned within 3 days picrotoxin was given for a further 48 hours because of the danger of relapse. Rovenstine (1938) found that, if there was no response to picrotoxin within 48 hours, the patient was unlikely to survive; if coma continued up to 48 hours, he persisted with picrotoxin for 3–6 days.

The ease with which a potential suicide may obtain large quantities of barbiturate, merely by going to a doctor with a story of "nerves" or insomnia, shows that the provisions of the Pharmacy and Poisons Act require strict implementation. Unless the patient is very well known to the doctor, the drug should be prescribed for a short period only, not to be repeated without further prescription. Lax prescription may help many along the road to self-destruction.

SUMMARY

The increasing frequency of death from barbiturate poisoning is emphasised.

The treatment of barbiturate intoxication is discussed, with special reference to the use of picrotoxin.

A case is described of recovery after taking gr. 115 (7·5 g.) of phenobarbitone and gr. 150 (9·7 g.) of aspirin.

I wish to thank Dr. Kenneth Perry for permission to publish the case-record.

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OUTBREAK OF SHIGELLA SCHMITZII INFECTION IN MEN AND APES

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SPONTANEOUS infection with *Shigella schmitzii* in any animal other than man appears to have been recorded only once by Fairbrother and Hurst (1932). This was in a rhesus monkey (*Macaca mulatta*), which had "spontaneous diarrhœa." Though this monkey appears to have been in close contact with others of the same species, no further spread was recorded.

Infection of primates with *Sh. flexneri* occurs more often. Thus Ravaut and Dopter (1909) in the rhesus monkey, Scott (1927) in the gorilla, and Lovell (1929a) in the Mozambique monkey (*Cercopithecus mossambicus*) found "Flexner bacilli" without recording the type. Fairbrother and Hurst (1932) found five cases of infection with *Sh. flexneri* type II (W) and three of infection with *Sh. flexneri* type I (V) in rhesus monkeys. Bernhardt and Markoff (1912) described "a small epidemic" of infection with *Sh. flexneri* Y in "lower monkeys." David and Schirl (1939) found *Sh. flexneri* of an anomalous type in two young chimpanzees. An interesting outbreak in Hamburg due to *Sh. flexneri* Y was reported by Bach et al. (1931). Five "meerkatzen," a German popular name for several members of the genus *Cercopithecus*, were involved originally, and the infection spread to all seven members of the family which owned them and to ten of their neighbours. Two children, aged 2 and 4 years, died of the disease.

Stadie (1930) considered "bacillary dysentery" to be common in primates but named no specific organisms. Monkeys died suddenly with no diarrhœa but with ulceration of the colon and sometimes of the ileum. In the chimpanzee and orang-utan, however, the clinical picture is identical with that seen in man.

So far as is known, the monkeys confined in the Zoological Gardens in Regent's Park have been free from infection with dysentery organisms for some years past, but during the war 1939–45 it was impossible to maintain the staff or the equipment to examine on the spot specimens from suspicious cases. An outbreak of infection with *Sh. flexneri* type 103 occurred among the rhesus monkeys in June, 1947, and was described by Rewell and Bridges (1948).

The outbreak of infection with *Sh. schmitzii* reported here occurred in November of the same year and was unexpected in view of the infrequency of such reports hitherto. Reasons are given below for believing that dysentery among primates may be more frequent than has been thought.

The Epidemic

On Nov. 3, 1947, a young adult female chimpanzee (*Anthropopithecus troglodytes*) became acutely ill, with collapse and the passage of blood and fragments of mucosa per rectum. She was 10 years old and had been born in the gardens and raised by hand from birth. She survived that night, but next morning her stools were very frequent and consisted almost entirely of fragments of mucosa with a little blood. Later in the day she collapsed and died. In her collapsed condition no medication was possible. At necropsy on the day of death the only abnormality found was an intense phlegmonous inflammation of the entire intestine from the upper jejunum to the lower rectum, most of the mucosa being sloughed off or hanging in shreds, leaving a raw and bleeding surface. The contents of the intestine consisted of blood and fragments of mucosa only. Cultures of the stools before death and of the gut contents at necropsy were made on MacConkey's agar, on desoxycholate-citrate agar, and in tetrathionate broth. From the desoxycholate-citrate-agar plate made in life an almost pure growth of *Sh. schmitzii* was obtained. After death only *Proteus morganii* was found.

The dead chimpanzee had been kept in a special section of the monkey-house reserved for the great apes, and screened from the public by a glass panel for fear of respiratory infections. Two keepers only entered by a special service corridor shut off from the rest of the house by a door. Each cage has its own drain, and all cleaning utensils are kept separate. The food is prepared in the same kitchen as for the other primates and consists mainly of raw fruit and vegetables. At the time of the outbreak the section contained five lar gibbons (*Hylobates lar*), which had arrived from Siam on Oct. 2, 1947, and were together in the cage next to the chimpanzee that died. There were also three young wild-caught chimpanzees, each in a separate cage; two spider monkeys (*Ateles virgatus*) in one cage; and two orang-utans (*Pongo pygmæus*) also in one cage. The spider monkeys had arrived in July, 1947, and one orang-utan in September, 1947. The other apes had been in the house for some years.

On Nov. 8, 1947, the senior keeper in the special section, aged 40, was taken acutely ill with cramping abdominal

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pain and diarrhœa, with the passage of blood and mucus per rectum. He stayed at home, and his doctor sent a stool to a local public-health laboratory, where no pathogen was isolated. The keeper returned to work on Nov. 14, but in view of his recent trouble a fæcal specimen was demanded. This, taken the same morning, contained much blood and mucus. *Sh. schmitzii* was isolated from it on desoxycholate-citrate agar. The man was kept off duty and given sulphaguanidine by mouth. He was ill on and off for some weeks, but no pathogen was found in his stools after Nov. 20. Eventually he made a complete recovery.

As a result of this finding a complete fæcal survey was carried out on the other apes in the special section and on the keepers in the whole house. On the death of the chimpanzee the five gibbons had been isolated from each other in separate cages elsewhere. Examination of their stools showed the presence of *Sh. schmitzii* in one. It was then remembered that this animal had passed frequent loose motions since arrival; but, since bowel upsets are common in recently arrived animals of all types, especially with the present restricted and poor-quality food, no notice had been taken of this. Moreover, this ape had been in captivity in Siam before being sent to England. Its former owner remembers similar trouble occurring during that period.

Of the seven men working in the monkey-house, *Sh. schmitzii* was found in the stools of the junior keeper in the special section aged 17. He confessed to loose motions for "some days," and this appeared to have started before the death of the chimpanzee but after the arrival of the gibbons. He did not know of any diarrhœa at his home, but it was impossible to examine the stools of his family. No mucus was found in the lad's stools, and the organism disappeared after a few days' treatment with sulphaguanidine.

Serological Examination

Serum obtained from the senior keeper on Nov. 18 showed no agglutination when tested against the standard suspension of *Sh. schmitzii*, but it agglutinated the group phase of this organism (strain Hawkins) to a dilution of 1 in 125. Of three human sera sent to the Dysentery Reference Laboratory, Oxford, for other purposes and tested at the same time, two were completely negative and one showed agglutination of the group phase only to a dilution of 1 in 50.

Serum obtained from the junior keeper on Dec. 8 agglutinated the standard suspension and the organism isolated from the dead chimpanzee to a dilution of 1 in 25. It agglutinated the group phase of *Sh. schmitzii* up to a dilution of 1 in 250.

These results are similar to those obtained when rabbits are immunised with *Sh. schmitzii*. A much higher titre is reached for the group phase than for the specific phase, even though the inoculum is entirely specific in character (Boyd 1935).

DISCUSSION

The most interesting point at issue seems to be the origin of the infection. Two possibilities seem likely: that it was introduced by the lar gibbon; and that it came from one of the infected keepers. The seclusion of the animals involved and the absence of infection among the other men makes it unlikely that the organism came from the junior keeper. It seems, therefore, that the infected lar gibbon had introduced the organism. In captive wild animals the carrier state has been observed with *Salmonella typhi-murium* in baboons (Scott 1926) and penguins (Cockburn 1947), though not apparently with dysentery organisms, unless a carrier stage was involved in the outbreak reported by Bach et al. (1931).

A small point of technical interest is that the pathogen was not recovered from the senior keeper by another laboratory. This man had received sulphaguanidine before any tests were made, and it appears that *p*-aminobenzoic acid was not added to the medium used, as was done when successful cultures were obtained.

A further technical point is that *Sh. schmitzii* was isolated from the fæces of the chimpanzee before death but not from the gut contents at necropsy. However, a non-lactose-fermenting organism was found on desoxycholate-citrate agar, but subculture from a single colony proved it to be *P. morganii*. This may be due to the difficulty of distinguishing between colonies of this organism and those of dysentery bacilli after only eighteen hours' incubation on the medium used, at any rate in a laboratory where many of the latter are not encountered.

A final consideration is the frequency of reports of outbreaks of enteritis in captive wild animals where accurate identification of the organisms involved was not made. Outbreaks in many different animals are encountered in zoological gardens, and it is obvious that many may be due to bacteria, viruses, or protozoa which are not known to be pathogenic to any other species of animal and so cannot be recognised as the cause of such trouble, unless extensive experimental work is done. For economic reasons alone this cannot be done with unusual animals.

As regards only in-vitro tests, however, much of the work done is incomplete, and some was done before the introduction of many modern aids in the identification of intestinal organisms. Thus, in a study of organisms from animals dying at Regent's Park, lists are given of biochemical and cultural reactions of organisms which were isolated but could not be identified. Some of these may well have been true dysentery organisms, but the reactions described, while allowing such a possibility, are not complete enough for exact diagnosis. Agglutination tests on these organisms were also incomplete by modern standards. Moreover, surveys on captive wild animals have always been spasmodic, and even at Regent's Park, where more emphasis is laid on pathology than in most collections, no bacteriological examinations whatsoever have been made during long periods.

The rôle of *P. morganii* in enteritis of lower animals has been much debated—e.g., by Lovell (1929b). It is always possible that in some cases *P. morganii* may have overgrown other organisms, as it did after death in the chimpanzee described above.

SUMMARY

Enteritis due to *Sh. schmitzii* broke out in apes and in men in close contact with them. The organism appears to have been introduced by a carrier, a lar gibbon. It caused the death of a chimpanzee, a severe attack of dysentery in one man, and transitory diarrhœa in another.

These findings are published by permission of the Zoological Society of London. I wish to thank Lieut.-Colonel R. F. Bridges, of the Dysentery Reference Laboratory, Oxford, for the identification of the organism and for the serological tests, and Prof. K. Schneider, of Leipzig, for sending me 'Photostat' copies of some of the references which are not available in this country.

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PLASMA-PROTEIN LEVEL AND DISAPPEARANCE OF EVANS BLUE FROM THE BLOOD-STREAM

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RAWSON (1943) showed that the dye Evans blue (T-1824), commonly used for determining plasma volume, migrated with the albumin fraction of blood-plasma in electrophoresis and ultracentrifuge experiments. This discovery, together with the results of parallel studies on the absorption of light by the dye in the presence of various plasma-protein fractions, led her to conclude that the dye was selectively attached to albumin. Gregersen and Rawson (1943) observed that dyes of different though similar chemical constitution, when injected into the blood-stream, disappeared at different rates, and they suggested that the rate of disappearance depended on the affinity of dye for plasma-albumin—the stronger the bond between the dye and the albumin the less the tendency of the dye to disappear from the blood-stream. LeVeen and Fishman (1947) have shown that Evans blue has a much greater chemical affinity for albumin than for any of the other plasma-protein fractions.

It might therefore be expected that in people with a low plasma-albumin level the dye injected intravenously would disappear more rapidly from the plasma. The plasma volume of patients with different degrees of hypoproteinæmia has already been determined by Walters et al. (1947b). The plasma-protein level was 2·9–7·5 g. per 100 ml., and the plasma-albumin 0·8–5·3 g. per 100 ml. If there is a change in the rate at which Evans blue disappears from the plasma of patients with hypoproteinæmia it should be revealed in the results of these experiments. Accordingly the data have been re-examined.

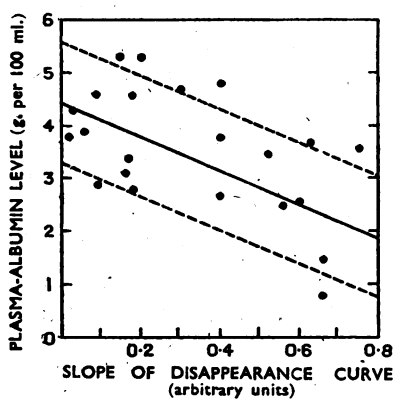

Fig. 1—Relation between slope of disappearance curve of Evans blue and plasma-albumin level: solid line, regression of plasma-albumin level on slope of disappearance curve; dotted lines, ± standard deviation.

Methods.—The subjects were all prisoners-of-war who had been held in captivity by the Japanese for 3½ years. The clinical condition of the patients and the techniques used have already been described (Walters et al. 1947a and b). The plasma volume was determined as soon as was practicable after the patients had been admitted to hospital. The dye was injected into one arm, and samples were withdrawn from the other arm after 10, 20, and 50 min. From the plasma-dye levels in these samples a disappearance curve for Evans blue was plotted and the plasma volume at zero time calculated. It was found that, whereas the disappearance curve was reasonably linear, the slope of the curve varied greatly from patient to patient.

In many of the patients the plasma-volume determination was repeated at regular intervals. The slope of the disappearance curve usually became less steep with each successive determination. This may have been due to a change in the plasma-protein level, which progressively increased as the general condition of the patient improved; but, since this change in the slope of the curve might possibly be the result of saturating tissues capable of storing the dye (Cruickshank and Whitfield 1945), the results of these subsequent determinations have been disregarded in the present analysis, the first determination only in each patient being considered.

Results.—The results are given in the accompanying table. There was a significant negative correlation (coefficient of correlation = − 0·602 ± 0·14) between the slope of the disappearance curve and the plasma-protein level—the lower the plasma-protein level the greater was the rate of disappearance of the dye. The plasma-albumin level was more important than the plasma-globulin level, since there was no significant correlation between the slope of the disappearance curve and the plasma-globulin level (coefficient of correlation = 0·145 ± 0·21); but the correlation between the slope of the curve and the plasma-albumin level (coefficient of correlation = − 0·602 ± 0·14) was the same as that between the slope of the curve and total plasma-protein level (figs. 1 and 2).

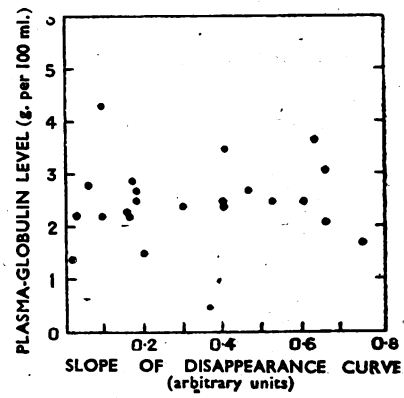

Fig. 2—Relation between slope of disappearance curve of Evans blue and plasma-globulin level.

DISCUSSION

Gollan (1947) has reported a similar result for infants with severe malnutrition. A negative correlation between the disappearance-rate of the dye and the plasma-protein level was described, but it was not stated whether the disappearance-rate of the dye was correlated with the albumin or the globulin fraction of the plasma-protein.

There is much confusion about the interpretation of the Evans-blue disappearance curve. It seems fairly well established that in man (Gibson and Evans 1937) and in the dog (Gregersen and Rawson 1943, Miller 1947) the fall in the plasma-dye level can be divided into

PLASMA-PROTEIN LEVEL AND SLOPE OF DISAPPEARANCE CURVE OF EVANS BLUE

Patient no.	Slope (arbitrary units)	Plasma-protein (g./100 ml.)	Plasma-albumin (g./100 ml.)	Plasma-globulin (g./100 ml.)
2	0·09	7·2	2·9	4·3
6	0·40	6·2	2·7	3·5
24	0·66	2·9	0·8	2·1
25	0·56	5·2	2·5	2·7
26	0·66	5·1	2·0	3·1
28	0·18	5·5	2·8	2·7
30	0·63	5·3	1·6	3·7
31	0·52	5·3	2·8	3·5
32	0·17	6·3	3·4	2·9
34	0·02	5·2	3·8	1·4
36	0·60	5·1	2·6	2·5
37	0·18	7·1	4·6	2·5
38	0·03	6·5	4·3	2·2
39	0·40	7·2	4·8	2·4
40	0·06	6·7	3·9	2·8
41	0·40	6·3	3·8	2·5
42	0·30	7·1	4·7	2·4
43	0·20	6·8	5·3	1·5
44	0·09	6·8	4·6	2·2
45	0·15	7·5	5·3	2·3
48	0·75	5·3	3·6	1·7
49	0·16	5·3	3·1	2·2

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three phases. Phase I is the "mixing curve" and lasts for 5 or 6 min. Phases II and III have been called the "disappearance slope" (Gibson and Evans 1937). Gregersen and Rawson (1943) have shown that this can be divided into an early "logarithmic phase" (phase II) lasting 1 or 2 hours and a later linear phase (phase III). Using cats, Cruickshank and Whitfield (1945) have also described a disappearance curve of three phases, with somewhat different time relations. Though there are obvious dangers in applying the results of experiments on animals to man, it seems probable that, since the slopes of the curves used in the present study were all calculated for the 10–50 min. period, the figures of the table represent the slope of phase II of the disappearance curve. It should, however, be pointed out that, with the dye concentration usually used in man, the points of transition between the various phases are far from sharp, and can be detected only if the number of samples taken far exceeds that which is usually possible in routine work.

Phase II of the disappearance curve has been interpreted differently by different workers. Rawson (1943) suggests that it may be a measure of the permeability of the capillary to albumin. Cruickshank and Whitfield (1945) suggest that it represents the absorption of the dye by some mechanism such as the reticulo-endothelial system. LeVeen and Fishman (1947) suggest that it represents the establishment of an equilibrium between free Evans blue and extra-circulatory tissue protein of an unspecified nature and site, but they do not exclude the possibility that this tissue protein may be, as suggested by Cruickshank and Whitfield (1945), protein of the reticulo-endothelial system. Miller (1947) suggests that phase II represents the diffusion of the dye into non-circulating plasma.

Since the slope of the disappearance curve depends so much on the plasma-albumin level, the suggestion of LeVeen and Fishman (1947) is the most attractive. The rate at which dye would leave the blood-stream to go to the tissue stores would depend on the relative affinities of the plasma-protein and tissue-store protein for Evans blue, and on their relative levels. If the plasma-protein level is low and the affinity of that protein for Evans blue also low because of a decrease in the albumin/globulin ratio, one would expect the dye to leave the blood-stream more quickly until such time as the tissue stores have been saturated—i.e., until equilibrium has been obtained.

Whatever is the cause of the more rapid disappearance of the dye from the plasma of patients with a low plasma-albumin level, the important practical point remains that, in the determination of plasma volume, curves representing the disappearance of dye from the blood-stream should always be made. The plasma volume should never, as has sometimes been suggested, be calculated from the result of one isolated estimation of plasma-dye level, especially if there is a possibility that the plasma-protein level or the albumin/globulin ratio is abnormal.

SUMMARY

There was a negative correlation between the slope of the disappearance curve of Evans blue, injected into the blood-stream of patients with different degrees of hypoproteinæmia, and the plasma-protein level. The correlation was entirely with the level of albumin and not with that of globulin.

In the determination of plasma volume by the dye method disappearance curves should always be plotted. The plasma volume should never be calculated from a single estimation of the plasma-dye level, especially when the plasma-protein level or the albumin/globulin ratio is abnormal.

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SUCTION APPLIED TO APPENDICECTOMY

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WITH the "interval" or uninfected appendix there is no danger of wound or peritoneal infection and no difficulty in holding the appendix, unless the surgeon decides to remove the appendix backwards. The procedure here described is designed for use with the appendix that is infected, œdematous, and often friable and difficult to hold—i.e., the appendix removed in an emergency—but it can be applied to the removal of almost any appendix.

Ficarra[1] advocated the use of a fingerstall over the appendix after it had been delivered and the meso-appendix cut (fig. 1). The fingerstall was held with a hæmostat applied to the base of the appendix. The main objection to this method is that the appendix inside the rubber fingerstall flops about and gets in the way, and, in common with most methods of wound protection, it is only after the appendix is delivered and the meso-appendix cut that protection can be applied.

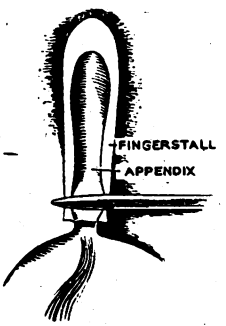

Fig. 1—Method of preventing contamination from an infected appendix as suggested by Ficarra.[1] The appendix is enveloped in a glove finger or similar rubber container.

It is during the delivery of the appendix through the wound that the danger of infecting the wound is greatest; once the appendix is outside the abdominal cavity and above skin level the protection of the wound is an easy matter, and any method may be used. Thus any method which aims to give the greatest protection to the wound must be applicable to the appendix while it is still inside the abdomen.

The tip of the appendix is usually its most inflamed part, probably because the blood-supply to the tip is poorer, the meso-appendix being usually absent here. Therefore if the tip presents or is anywhere near the peritoneal incision it can be engaged in the suction tube described below without undue interference by the meso-appendix.

When the tip of the appendix cannot be seen or brought near the wound without spreading infection in the abdominal cavity, it must be seriously considered whether, with the complete protection of the severed base afforded in the procedure described below, and the greater ease thus provided for retrograde dissection, it is not better to remove all such appendices backwards. Retrograde dissection secures the blood-supply early and works from the least infected part of the appendix, the base, where the planes of separation are easiest to find, to the most infected part, the tip, where the proper planes of cleavage are hardest to find, and where adhesion and infection are greatest.

The use of the suction tube in retrograde appendicectomy assists the surgeon in his dissection of the tip, the smooth round end of the tube finding the right planes for him as the appendix is slowly sucked up.

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As is done with the gall-bladder, it may become the custom to remove the very infected appendix from the base distally. The objection hitherto has been the possibility of infection from the distal cut end of the appendix.

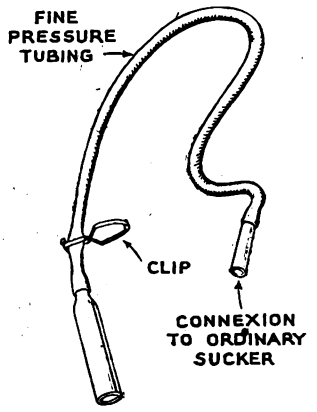

Fig. 2—The apparatus required.

TECHNIQUE

As soon as the tip (or base, when the appendix is removed in a retrograde manner) presents one of a series of tubes of different sizes is applied to it, and, by means of fine pressure tubing connected to the ordinary operating-room source of suction, the appendix is gently sucked into the tube and held by suction controlled by a spring and a screw clip (figs. 2 and 3*a*).

Next, the meso-appendix is dealt with in the usual way by "mass ligation" or clamping with hæmostats. Further suction is used to suck the appendix into the tube as far as the base, where it is prevented by a hæmostat from going further (fig. 3*b*).

When the appendix is to be removed backwards, the meso-appendix near the base is pierced with an aneurysm needle or curved hæmostat. Then, with the double tie thus introduced, the appendicular base is crushed and tied in the usual way, and the second ligature is tied about $^1/_3$ in. distal to the first, instead of a distal clamp, and the appendix is divided between the two ligatures. The distal cut end of the appendix is immediately engaged in the suction tube (fig. 5). Carbolic or other antiseptic may be applied to the appendical base on the cæcum, and this turned in with a purse-string or Z suture. Next, the appendix is held on tension with the suction tube, and the meso-appendix is divided above hæmostats. With each snip of the scissors on the meso-appendix more and more of the appendix is sucked up into the suction tube. Thus the appendix brings up with it the distal part of the meso-appendix, allowing of easier clamping and cutting.

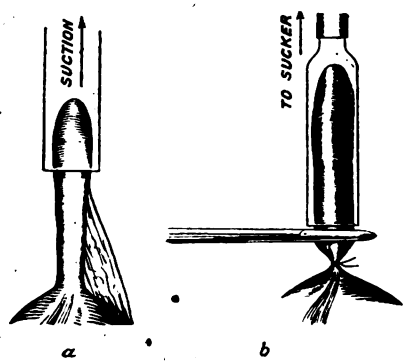

Fig. 3—Method of suction: *a*, if the tip of the appendix presents it is first engaged in the sucker as far as the meso-appendix; *b*, after the meso-appendix has been divided, further suction draws the appendix up so that it is covered as far as a hæmostat on the base.

When the meso-appendix has been completely removed, the distal part of the appendix—that part where infection is usually greatest and adhesions most difficult to separate, and where the appendix is usually most friable—can often be slowly sucked into the tube with little help from the surgeon. The rounded end of the suction tube separates the adhesions in the correct plane, helped by an occasional touch with a blunt dissector or scissors. Once started in the right plane—the plane of least resistance—the equalised hydrostatic pressure forces the end of the tube continuously along in the chosen plane of cleavage.

Stainless steel, plastic, and rubber tubes have been tried, but glass has been favoured because of its simplicity of manufacture and cheapness. Even if they are broken when being sterilised, glass tubes are soon replaced. Being transparent they allow the whole length of appendix being removed to be seen. As a standard tube for most cases the straight tube is best; but, where the base has to be tied deep in the wound, a curve at the end of the tube facilitates "getting round the point," just as a curve at the end of a long hæmostat facilitates tying-off vessels deep in a wound (fig. 4).

A series of three or four tubes are sterilised ready at operation. A tube of internal diameter greater than the thickness of the appendix is still effective—suction still holds the appendix in it—but the air rushing past the appendix may offend the surgeon's ear. An appendix slightly thicker than the internal diameter of the tube accommodates itself on suction to the tube. A tube length of 7 in. has proved adequate, and an internal diameter of $^3/_8$ in. is satisfactory for the average case. A set of five tubes of internal diameters $^5/_{16}$, $^3/_8$, $^7/_{16}$, $^1/_2$, and $^3/_4$ in. is advised.

The extension suction tubing can be quite thin and light, since slight suction only is needed. Where the appendix completely fills the tube, the suction system is static and the suction vacuum not seriously affected by the internal diameter of the tube.

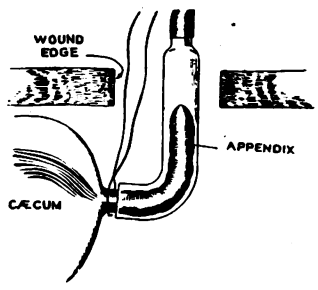

Fig. 4

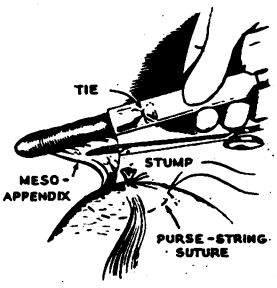

Fig. 5

Fig. 4—A curved tube is helpful when the base of the appendix will not deliver through the wound, and when the base must be tied in the depth of the wound.

Fig. 5—Removal of the appendix in a retrograde manner, the distal cut end of the appendix being held in the sucker tube while the meso-appendix is clamped and tied. Further suction then draws the whole appendix slowly into the suction tube, and assists in dissecting off any adhesions at the tip.

DISCUSSION

The advantages of this use of suction are as follows:

(1) The tip of the appendix, which is usually the most infected, can be isolated from the wound and peritoneal cavity from the time when it is first seen by the operator.

(2) The most friable of appendices, whether gangrenous or not, can be securely and safely held during the operation. Any part of the appendix broken off or any pus spilt goes into the suction tube, where it contaminates nothing and does no harm. There is no worry of "breaking it off" or of its "bursting."

(3) Retrograde removal of the appendix becomes just as free from the risk of wound contamination as forward removal, and in many cases more desirable, since the blood-supply is secured early and the most infected part of the appendix is sucked in last with least intra-abdominal handling.

(4) In either forward or retrograde removal the suction tube helps to dissect off adhesions in their right plane and thus assists the surgeon. This method should be easily applicable by those surgeons who like to remove the appendix subperitoneally.

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Disadvantages to be considered are that the method adds to the already large variety of instruments used by the surgeon in an appendicectomy—if only by a glass tube and a length of rubber tubing. A further possible disadvantage is that, when suction has been used, even a normal appendix may become so congested that the pathologist may have trouble in distinguishing it as a normal one.

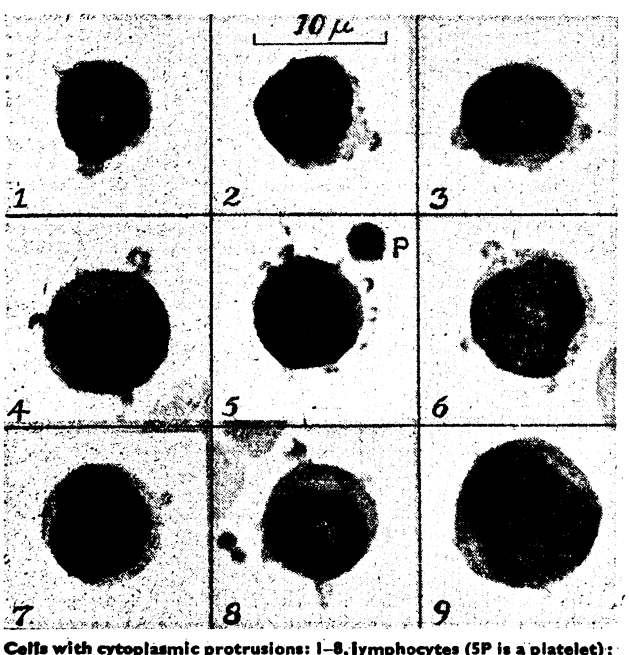
Clinical experience with the method in over twenty cases has so far not been sufficient for a statistical study of its effect on the incidence of wound infections to be made. But the method has certainly facilitated the removal of the very inflamed, friable, or gangrenous appendix, and has abolished the worry that the appendix may rupture or spill before it can be got out. The procedure should appeal to the occasional surgeon who is faced with either an "overripe" appendix or one which, on dissection, "disappears out of sight" in the retrocæcal or pelvic regions.

My thanks are due to Mr. Russell Grimwade, who spoke to me of the advantages of a "suction chuck" in lathe work.

Preliminary Communication

LYMPHOCYTES AND INTRAVASCULAR HÆMOLYSIS

THE work of Murphy and Sturm (1925), Ehrich and Harris (1942), and Harris et al. (1945) points to the lymphocytes as the probable source of the immune antibodies concerned in the response of experimental animals to bacterial infections. Kass (1945) has demonstrated gamma-globulin in human lymphocytes obtained from lymph-nodes excised an hour after death. Ehrich (1946) and White and Dougherty (1946) have shown that both normal and immune globulins, including gamma-globulins, are contained in the cytoplasm of the lymphocytes of laboratory animals and are released in the germinal centres of lymphoid tissue by the development and shedding of small cytoplasmic protrusions or buds. A similar budding process was observed in lymphoid tissue by Downey and Weidenreich as long ago as 1912, and this may be one way in which lymphocytes are normally destroyed in the body.



Cells with cytoplasmic protrusions: 1–8, lymphocytes (5P is a platelet); 9, cell with monocytic type of nucleus.

Evidence for the intravascular hæmolytic action of immune gamma-globulins adsorbed on the red-cell surface of patients with cryptogenic acquired hæmolytic anæmia (type Hayem-Widal) was presented from these laboratories by Boorman et al. (1946), who showed that washed red cells from five such patients were agglutinable by an anti-human-serum rabbit serum (containing an anti-human-gamma-globulin component) of the type described by Coombs et al. (1945a, 1945b, 1946) in connexion with the serological diagnosis of hæmolytic disease of the newborn.

We have recently studied a patient with Hodgkin's disease accompanied by a severe acquired hæmolytic anæmia conforming to the clinical and hæmatological criteria for the diagnosis of the Hayem-Widal type of anæmia; a full account of this case will be published shortly. In addition to the customary findings, the washed red cells were agglutinable by anti-human-serum rabbit serum, transfused normal red cells were rapidly eliminated, and methæmalbumin was present in the plasma, as was found in the cases described by Loutit and Mollison (1946).

Air-dried films of this patient's peripheral blood stained with Jenner-Giemsa showed many lymphocytes with small cytoplasmic buds in various stages of development. These buds were seen in as many as 25% of the lymphocytes in films made when the hæmolysis was particularly intense. Most of these cells were medium-sized lymphocytes, though such buds were also seen in large and small lymphocytes; occasional cells with a monocytic type of nucleus showed similar cytoplasmic protrusions. It seems reasonable to suppose that these buds were about to become detached from the cytoplasm of the parent cells, and that the globulins thereby released into the plasma might have included an anti-human-erythrocyte immune gamma-globulin component responsible for the intravascular destruction of this patient's red cells.

I am indebted to Dr. W. G. Millar for the photomicrographs.

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South London Blood Supply Depot,
Sutton, Surrey.

R. H. TRINICK
M.B. Belf.

". . . In a recent Washington Report on the Medical Sciences it is stated that the 'Army medical department is industriously gathering information on the establishment and operation of its own medical school.' . . . In its favor would be the fact that once established, it would at least provide a group of men who had committed themselves to a career in military medicine . . . a nucleus round which civilian physicians would gather in times of emergency. It might also lead to an eventual recognition of the importance of military medicine among medical educators as a whole. On the other hand the Army's present plan of assigning a medical officer to the faculty of existing medical schools on a coöperative basis might be developed to give quicker and larger results, and at a lower unit cost to the Government . . . . An alumni body could not aggregate into useful volume before 1960 at the earliest, and the accumulation of . . . tradition . . . would lie still further in the future . . . . the Army has been conspicuously successful in extracting the best available talent from the profession as a whole when it was needed and in as sufficient volume as can ever be permitted by the exigencies of war."—Leading article, *New Engl. J. Med.*, Jan. 6, p. 37.

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Reviews of Books

Development of Modern Medicine

RICHARD HARRISON SHRYOCK, professor of American history, University of Pennsylvania. London: Gollancz. 1948. Pp. 368. 21s.

THE history of medicine from the earliest times up to the present has often been told; but this is perhaps the most comprehensive attempt recently made to describe the development of medicine from the 18th century onwards. It shows that medicine has suffered much from its professors, as well as from the more ignorant laity. In the days of classical Greece, though medicine was primarily a priestly craft, healing of the body went hand in hand with healing of the soul. But as all advance in human history has been followed by periods of recession, so it has been with medicine: the hand of the Church was laid heavily on progress in experiment and research; nor were the universities, wedded as they were to Galen and Aristotle, any more helpful. It was not until the 15th century that the benefits of the Renaissance began to show in medicine; and 200 more years had to pass before there was any further development. The 18th century, however, was an era of enlightenment; and the author pays tribute to the pioneer work of Haller in physiology, and that of Morgagni, who laid the basis of modern pathology. On the surgical side he lays special stress on the influence of John Hunter, who found surgery a mechanical art but left it an experimental science. The development of the public-health movement in this country and in America is fully discussed. Sanitary reform did not impress the public, and the reputation of the medical profession was at a low ebb and remained so until its prestige was restored by the triumphs of bacteriology.

Gynæcological Histology

JOSEPHINE BARNES, M.A., D.M. Oxfd, M.R.C.P., F.R.C.S., M.R.C.O.G., assistant, obstetric unit, University College Hospital, London. London: Harvey & Blythe. 1948. Pp. 242. 30s.

Miss Barnes has given much time and care to producing this handbook for students of gynæcology. The text is clear and simple, though many gynæcologists will disagree with a few of the more didactic statements, as Miss Barnes herself predicts in her preface. The microscopical sections and views are well chosen and on the whole depict sufficient detail for the student, though sometimes cell and nuclear detail is obscured by overstaining. Many of the photographs are good, as will best be realised by those gynæcologists who have themselves attempted work of this type. The very-low-power pictures, always a difficult problem, have not reproduced well. We cannot help regretting that Miss Barnes should present yet another classification of ovarian tumours to confuse the student, especially when he finds that the "sex-cell group" are classified as "epithelial." Her book, however, will prove useful to students preparing for examinations, and to clinicians studying for higher degrees.

Contemporary Religious Jurisprudence

I. H. RUBENSTEIN of the Illinois Bar. Chicago: Waldain Press. 1948. Pp. 120. $2.50.

Mr. Rubenstein's *Contemporary Religious Jurisprudence* casts its net wide. The religions which he discusses include not only fortune-telling, faith-healing, and quack doctoring but also the beliefs of conscientious objectors and mere simple pacifists. If his preface seems somewhat militantly to lump all these together as a menace to public welfare, health, morals, and national safety, the rest of his book refers dispassionately to the relevant statutes and judicial decisions of the U.S.A. (State and Federal) and of England and the Commonwealth countries. Among other items of information we learn that many American States check fortune-telling by requiring exponents of that art to pay a substantial annual fee (as high as $500 in West Virginia) for a licence to practise it. An intriguing decision is cited from the courts of Texas: when a woman claimed damages from a railway for its alleged negligence, counsel for the defendants sought to cross-examine her so as to establish that she was a Christian Scientist, and therefore, by reason of her belief, incapable of sustaining physical injury or mental suffering. Disallowed in the trial court, the cross-examination was held proper on appeal. Mr. Rubenstein observes that the ruling would equally apply to Christian Scientists claiming damages for slander or for breach of promise of marriage.

The English cases are well summarised. We still rely upon the Act of 1735 for dealing with "such persons as pretend to exercise or use any kind of witchcraft, sorcery, inchantment or conjuration." As recently as 1944, in R. *v.* Duncan, our courts were discussing the meaning of "conjuration" where a professional spiritualist medium was engaged at a substantial fee to give séances in a "temple" over a chemist's shop. We still employ, too, section 4 of the Vagrancy Act of 1824 which is aimed against persons "pretending or professing to tell fortunes or using any subtle craft, means or device, by palmistry or otherwise, to deceive or impose on any of His Majesty's subjects." It is not necessary here to prove a fraudulent intent, but there must be an individual affected: in Barbanell *v.* Naylor (1936) a newspaper's daily forecast of the fortunes of people born on a particular day ("What the Stars Foretell") was held to be addressed too generally to be within the statute. Naturally Mr. Rubenstein is largely concerned with elements of jurisprudence which are special to his own country—e.g., the defence of constitutional religious freedom recognised by fundamental law, and the restriction by Federal statute of the use of the mails to defraud. But his book contains much matter of general interest, particularly in his second chapter which deals with the medicolegal aspects of faith-healing.

Recent Advances in Anæsthesia and Analgesia (6th ed. London: J. & A. Churchill. 1948. Pp. 215. 21s.).—Dr. Langton Hewer has included fresh information on a host of new subjects, needing 34 additional illustrations. This edition, continuing the tradition of former ones, remains one of the best reference books on present-day clinical anæsthesia. Further important examples of the wide range of new subject matter are: the mechanics of direct vision laryngoscopy, intramedullary anæsthesia and infusion, brachial-plexus block, resuscitation by arterial transfusion, skin temperature of the forehead as a sign of shock, and recent knowledge of pulmonary embolism. Every anæsthetist, expert or in training, will find this book invaluable.

Neuroanatomy (2nd ed. London: H. Kimpton. 1948. Pp. 539. 50s.).—This textbook, by Prof. Fred A. Mettler, of New York, was well received when first published in 1942, and has become justly popular with postgraduate students of neurology. The second edition has much the same form, but has sixty more pages; and like everything else has grown a good deal more expensive. It is still very good value; the use of three-dimensional pictures and of diagrams to illustrate the arrangement of meninges, blood-vessels, and nervous structures makes points clear which are often obscured by description. It is probably impossible to make light reading of the anatomy of the nervous system, but the serious student will not resent the detailed descriptions, and the more casual seeker will use the abundant pictures. Excellent indices of subjects, authors, and sources make reference easy. The second edition will be as widely used as the first.

A Textbook of Clinical Pathology (3rd ed. Baltimore: Williams & Wilkins. London: Baillière. 1948. Pp. 1023. 50s.).—This textbook, originally produced by Kracke and Parker, now bears only the name of Prof. Francis P. Parker, of the University of Virginia; and he died during its preparation. Eight authors, all experts in their own field, are responsible for the contributions. As before, Dr. Kracke writes on disorders of the leucocytes; and the other chapters include disorders of the erythrocytes, blood-groups, blood parasites, clinical blood-chemistry, assays of vitamins and hormones, renal and hepatic function tests, diagnosis of venereal lesions, and serological tests for syphilis. A useful appendix gives notes on topics ranging from the use and care of a microscope to preparation of culture media. As is common in American textbooks, English work is somewhat neglected; but the book can be recommended to students as well as to laboratory workers, and particularly to those not well acquainted with the American literature.

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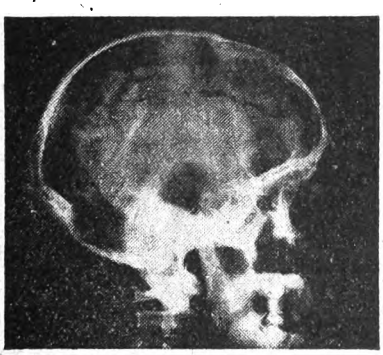
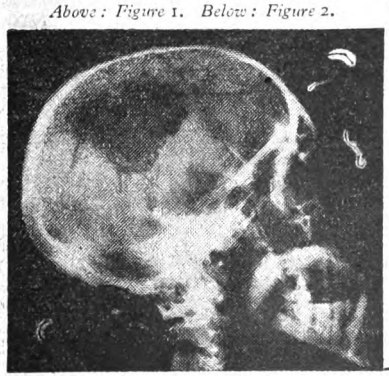


Above: Figure 1. Below: Figure 2.



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R. J. Age 49. Motor cycle accident. Admitted in deep coma, with large scalp wound and contusion over right temporal and parietal region.

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Feeding by indwelling naso-pharyngeal catheter carried out during period of semi-coma.

These details and illustrations are of an actual case. T. J. Smith & Nephew, Ltd., of Hull, manufacturers of Gypsona P.O.P. and Elastoplast bandages, publish this instance — typical of many — in which their products have been used with success.

Figure 3.

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THE LANCET

LONDON: SATURDAY, FEB. 5, 1949

Periodic Examination in Cancer Control

FOR some time there has been a school of thought advocating regular medical examinations as the best means of securing the early diagnosis of cancer, but hitherto few experiments have been made to prove or disprove this view. Regular medical examinations are a condition of membership of the Pioneer Health Centre at Peckham, and there 1500 examinations revealed only 2 unsuspected cancers; but the members are hardly a fair sample, being, in general, on the young side of middle age. Now MACFARLANE and her colleagues [1] at the department of gynæcology of the Women's Medical College of Pennsylvania have described an investigation, started in 1938 and 1939, in which 1319 white women between the ages of 30 and 80, and presumably healthy, volunteered to have a pelvic examination twice a year for 5 years. After the first enthusiasm some of the volunteers did not attend, others died, and still others left the neighbourhood, but the final report deals with the examination of 732 volunteers over 10 years. The results have been curious: the first examination of the 1319 women disclosed three unsuspected cervical cancers, although all had supervened on an already existing cervical erosion; radium was given with no recurrence in 9 years. A fourth cervical cancer was discovered at the eleventh visit of one of the volunteers. Here there had been no previous symptoms, but treatment was followed by severe complications, and the patient died of recurrence within 2 years. Four other cancers were discovered during the investigation—one each of the ovary and vaginal wall, in which treatment failed, and two of the corpus uteri, one of these patients being still alive 6 years after treatment whereas the other, in whom the disease was discovered at the first examination, died from recurrence after 9 years. These eight cancers occurred among the 732 women who stayed the 10-year course, an incidence of 1·1%; if cancers of the cervix are taken by themselves the proportion is 0·54%. This makes an interesting comparison with the 57 cervical cancers discovered among a random sample of 3000 patients aged 30–80 admitted to the gynæcological wards. MACFARLANE claims that, apart from the detection of early cancer, her examinations have revealed 214 inflammatory lesions of the cervix, the elimination of which has sometimes prevented the development of malignant changes.

What is the lesson of this experiment? Should everyone be advised to undergo regular medical examinations to detect early cancer, not only in the pelvis but in the whole body? There is no doubt that cancer has an immensely greater chance of cure if it is treated early and that the proportion of patients first seen when their disease is at an early stage is deplorably small. But are periodic medical examinations the best way of raising this proportion? Some of the difficulties which cancer-detection clinics have to face are set out by WESTING [2] of New York. Since malignancy may arise at any age, and since there is still no accepted single test for the presence of cancer, every organ of every person would have to be examined periodically from birth onwards. Even if the examination was confined to the deep organs WESTING estimates that to examine the whole population once a year would occupy every doctor in the U.S.A. for an average of 5 hours a day. He cites the experience of GOLDMAN [3] at one such clinic, where 6 specialists and 6 non-medical assistants spend 4 hours weekly in examining 16 people: at this rate the clinic will watch over the health of about 800 people. Apart from the large number of doctors and technicians, the amount of equipment, and the extension of premises that would be needed for such a service on a national scale, there is the inevitable danger that in such a scheme too much emphasis will be laid, in the public mind, on ill health. People may come to rely so much on these regular examinations that they will no longer take an intelligent interest in keeping themselves well and in noticing small but significant deviations from the normal.

The realisation that increasing years, while inevitably bringing a diminution of powers, do not necessarily bring discomfort and disease, and that bowel disturbances, flatulence, heartburn, vaginal discharge, and like ills are not the normal concomitants of old age but signs that something is wrong, may well do more good than occasional overhauls, however thorough. WESTING would like to see the general practitioner examining the breast and uterus of all his female patients of cancer age once or twice a year. To this could perhaps be added an annual examination of the mouth and rectum, and an examination of fæces for occult blood, in all patients over 35. All agree that the doctor needs to become more conscious of the presence and curability of cancer, and should ever be on the watch for those seemingly unimportant symptoms which now and again will disclose the early cancer.

Toxamins and Anti-vitamins

IT has long been known that some foods contain substances which interfere with the action of vitamins, and in the last few years numerous synthetic analogues of the vitamins have been found to have the same effect. Research on these factors has been advancing rapidly, and the conferences held by the National Centre for Scientific Research in Lyons and by the Nutrition Society in London have been useful in collecting and coördinating a mass of widely scattered knowledge. As L. J. HARRIS has pointed out, the existence of anti-vitamins was postulated in the earliest days of vitamin research. Thus EIJKMANN, in his pioneer studies on polyneuritis in fowls, assumed that the polished rice on which they were fed contained some toxic substance which could be counteracted by an antidote located in the polishings. This view was proved incorrect, in the sense originally intended,

1. Macfarlane, C., Sturgis, M. C., Fetterman, F. S. *J. Amer. med. Ass.* 1948, 138, 941.

2. Westing, S. W. *N.Y. St. J. Med.* 1949, 49, 51.
3. Goldman, L. B. *J. Amer. med. Ass.* 1947, 135, 276.

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when GOWLAND HOPKINS showed that diseases may be caused, without the intervention of toxic agents, merely by deficiency in nutrients needed in minute amounts. Later research, however, has indicated that the body's requirements for aneurine (B_1) are related to the carbohydrate intake; and on this basis the starch in polished rice might be looked on as toxic to fowls suffering from aneurine deficiency. Apart from these early surmises, MELLANBY must be given full credit for the introduction and practical proof of the "toxamin" theory. About 20 years ago he found that dogs whose diets contained certain cereal products—particularly oatmeal—were abnormally liable to rickets. BRUCE and CALLOW subsequently showed that the anti-calcifying properties of cereals were due to the presence of phytic acid, which is a phosphorylated form of the vitamin inositol. HARRISON and MELLANBY confirmed that phytic acid had the same rachitogenic effects as cereals in dogs, while MCCANCE reported that calcium metabolism was disturbed in human subjects subsisting on a diet consisting largely of wholemeal bread, which is rich in phytic acid.

Investigations in many other fields have since demonstrated that a wide variety of natural substances may interfere with the action of different vitamins. Thus vitamins A and E are opposed by rancid fats, vitamin E by cod-liver oil, vitamin K by dicoumarol present in spoilt sweet clover, vitamin B_1 by some forms of raw fish and by substances present in ferns, nicotinic acid by maize, and biotin by the avidin present in raw egg-white. In addition to these natural antagonists many artificial anti-vitamins have been synthesised. The first representatives of this class to be discovered were the sulphonamides, which were used in infections before their biological significance was fully understood. The WOODS-FILDES theory that they exert their bacteriostatic action by competition with *p*-aminobenzoic acid, and the later recognition of this substance as a vitamin either by itself or as a component of pteroylglutamic acid, have now amply justified the classification of these well-known therapeutic agents as anti-vitamins. Artificial anti-vitamins opposing the actions of vitamins B_1, C, E, K, nicotinic amide, riboflavine, biotin, adermin, pantothenic acid, inositol, and choline have been synthesised. Some of the vitamins they antagonise are no less important than *p*-aminobenzoic acid for the nutrition of bacteria, but few of the anti-vitamins so far tested show promise of rivalling the sulphonamides in the treatment of infections. Their mode of action appears to depend on their close chemical similarity to the actual vitamins, which allows them to displace the vitamin in its association with essential enzyme systems, thus rendering these systems ineffective. Clearly, therefore, the artificial analogues must differ widely in their mode of action from most of the naturally occurring antagonists, which seldom bear a close chemical resemblance to the vitamins which they oppose. KODICEK contends that the term "toxamin" should be applied to all substances which interfere with the action of vitamins, whereas "anti-vitamin" should be reserved for the substances which act by reason of chemical analogy. On this basis dicoumarol, which was discovered in spoilt sweet clover through the severe outbreak of hæmorrhagic disease which it caused in cattle, may reasonably be classed as a naturally occurring anti-vitamin; and incidentally the use of dicoumarol in the treatment of thrombosis is an instructive illustration of the application of veterinary research to human medicine.

The existence of toxamins adds greatly to the perplexities of the analyst called on to estimate the vitamin values of a food. For most vitamins he has both chemical and biological methods of testing at his disposal. If he uses chemical tests he will learn how much of a particular vitamin is present, but he will not know whether the vitamin can be efficiently absorbed from the food or whether the food contains toxamins which will prevent the vitamin from exerting its full activity. A biological test, on the other hand will measure the total physiological activity of the food, as influenced by the efficiency of absorption of the vitamin and the presence or absence of toxamins, but will not tell him the actual amount of vitamin present. Measurements of "vitamin contents" by chemical methods and of "vitamin activities" by biological methods, therefore, may sometimes give widely divergent results. Neither result can be considered more essentially right than the other, and the choice will depend on the question which the analyst has set out to answer. To avoid ambiguity, data on the vitamin values of foods should be accompanied by an indication of the method of estimation used.

Histoplasmosis and Pulmonary Tuberculosis

THE resemblance between tuberculosis and some fungus infections of the lung has long been recognised, particularly in the United States. Coccidioidomycosis, for example, can sometimes only be distinguished from tuberculosis by careful examination of the sputum and the specific skin-tests to tuberculin and coccidioidin; while torulosis, as DANIEL and his colleagues [1] lately showed in these columns, can simulate tuberculosis of the nervous system very closely. No condition recognised by mycologists has given rise to such intense speculation within recent years as histoplasmosis, an infection with the fungus *Histoplasma capsulatum*, which is sometimes known as "Darling's disease," the acute form of which has been known since 1906. The early cases recorded presented with fever, ulceration of the mouth and gastro-intestinal tract, enlargement of the liver, spleen, and lymph-glands, anæmia, and leucopenia. It was confused with kala-azar until the causative organism was found either in the blood or more often in affected tissue, particularly the lymph-glands and bone-marrow. Isolated reports appeared subsequently, but the real extent of the infection did not begin to be suspected until 1945, when CHRISTIE and his colleagues [2] in Tennessee, after observing a fatal case in a child, prepared histoplasmin, a substance which on injection produced a specific skin reaction in people who had been infected with the fungus. Further studies showed that histoplasmin sensitivity was unexpectedly common; that such sensitivity was sometimes associated with pulmonary calcification, usually multiple and sometimes massive but often miliary in type; and that many people with dis-

1. Daniel, P. M., Schiller, F., Vollum, R. L. *Lancet*, Jan. 15, p. 53.
2. Christie, A., Patterson, J. C. *Amer. J. publ. Hlth*, 1945, 35, 1131.

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seminated pulmonary calcifications reacted positively to histoplasmin but not to tuberculin. Furthermore, sensitivity to histoplasmin seemed to be more or less confined to a rigid geographical area in the Middle West of the U.S.A. Since most of the histoplasmin reactors gave no past history of illness it is evident that infection with the fungus can occur in a subclinical form: there appears, in fact, to be a gradation in severity from the acute generalised histoplasmosis described by DARLING to the subclinical form, inferred from the results of skin testing which may or may not be associated with multiple calcifications in the lung substance. For example, in five cases which came to necropsy HOLT [3] has noted lung changes ranging from miliary parenchymatous lesions, with hilar lymph-glandular enlargement, to patchy pneumonitis and larger areas of pulmonary consolidation.

The many writers on this subject in the last five years have emphasised the close similarity between histoplasmosis and tuberculous infection; they have also cast doubt on the fairly general assumption that calcified deposits in the lung substance, symptomless and discovered accidentally by X ray, are always the result of tuberculosis. But calcification, even though symptomless, is the end-result of a previously active focus, and such foci in histoplasmosis have only rarely been recognised and studied. EDWARDS and colleagues [4] have now tried to bridge this gap in a detailed and comprehensive study of the pulmonary infiltrates and mediastinal lymph-glands enlargement observed among 12,803 student nurses who were systematically tested for sensitivity to both tuberculin and histoplasmin. Of these nurses 224 showed pulmonary infiltrates, classified into (1) nodular, (2) poorly circumscribed, (3) fibrotic, and (4) "non-specific" infiltrates, naturally of diverse ætiology. Only 0·26% of the infiltrates were found in the group which reacted to neither antigen. Further analysis revealed an association between the type of infiltrate and the type of antigenic sensitivity. Thus, for nodular infiltrates, among nurses who reacted to histoplasmin alone the rate was 3·4%; whereas among the tuberculin reactors who did not react to histoplasmin it was 0·4%. The opposite was true of poorly circumscribed infiltrates, which were found in 1·9% of nurses who reacted to tuberculin alone compared with 0·4% of those reacting to histoplasmin alone. Other points of difference suggested by this survey were: first, that the poorly circumscribed infiltrates associated with a positive tuberculin reaction tended to occupy the upper parts of the lungs, whereas the nodular infiltrates found in histoplasmin reactors were universally distributed; and secondly, that calcification seemed more common in the nodular infiltrates of the histoplasmin reactors than in the other groups. Enlargement of the mediastinal lymph-glands was observed 38 times: 31 of these nurses reacted to histoplasmin alone, 4 to both antigens, and 3 to neither antigen. None reacted to tuberculin alone.

These studies should not be regarded as supplying final proof, but they forcibly suggest that histoplasmosis in the United States is a disease to be reckoned with as a source of pulmonary calcification. On this side of the Atlantic the infection has not yet been demonstrated, so far as we are aware: of several hundred people living in Holland none were found to react to histoplasmin,[5] and a small investigation by MCWEENEY and his colleagues [6] on 320 Dublin children was completely negative. We must nevertheless be on the watch.

3. Holt, J. F. *Amer. J. Roentgenol.* 1947, 58, 717.
4. Edwards, L. B., Lewis, I., Palmer, C. E. *Publ. Hlth Rep. Wash.* 1948, 63, 1569.
5. Quoted by Christie and Patterson.
6. McWeeney, F. J., Crowe, M., Dunleavy, E., Magnon, M. *J. med. Ass. Eire*, 1946, 19, 163.
7. *Manchester Guardian*, Jan. 12, 1949.
8. *Lancet*, 1947, i, 571.
9. *Ibid*, 1942, ii, 221, 340.

Annotations

THE WRONG DRUG

DOCTORS and nurses are still not always fully aware of the potency of the local anæsthetics they handle every day, and of the ease with which these drugs, improperly used, can kill. Distressing and needless deaths still occur in our hospitals—and not by any means only in the smallest ones—because a drug is injected either in mistake for another or in gross overdosage. One of the common mistakes is to inject a more potent local anæsthetic (the names of all of them end in ". . . caine") in the belief that it is procaine. The drug is injected in a dose many times its proper one, and the patient dies. Lately another such report [7] has been added to the already long list of similar cases. A young man was to have a nasal operation. A liquid which the surgeon believed to be procaine was injected. It was in fact cocaine and the patient died. Once again the coroner expressed the hope that, to avoid a repetition of this accident, drugs would be identified by distinctive colours and those responsible for them would be more careful. But neither publicity nor coroners' admonitions have sufficed to prevent these distressing errors. The injection of cocaine instead of procaine is but one example of mistaken identity. Alcohol and thiopentone, as well as antiseptics of various kinds, have also been injected, instead of local anæsthetics, into nerves, with disastrous results. Even the fear of litigation, and the possibility of heavy damages such as have been imposed in another case of this nature,[8] have not been effective. In the long run the only remedy lies in teaching medical students the dangers of these drugs and the dire results that follow their confusion. At present students, and even budding surgeons, receive little instruction on local anæsthetic drugs apart from what they are taught by professional pharmacologists early in their career. It might be better if this information was given them shortly before their qualification by someone familiar with the drugs through daily use.

In the case of local anæsthetics the two suggestions commonly put forward are for the solutions to be distinctively coloured, and for the names of the drugs to be so dissimilar in sound that they could not be confused even in the most indistinct telephone conversation. Either suggestion would undoubtedly help to prevent accidents if adopted on a national scale, with the backing of the *British Pharmacopœia* and defence societies, and if non-observance carried legal penalties. But many hospitals already colour their cocaine red; and at least one death occurred because the pharmacist omitted to do so and the solution was assumed to be procaine. To reduce the chances of error precautions of this sort must be backed by a heightened awareness of the possibility for danger. It is still not uncommon, for example, to hear 'Nupercaine' referred to as 'Percaine' at scientific meetings, though the latter name was given up some six years ago [9] because there had been confusion between percaine, cocaine, and procaine. Then if "dangerous

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drugs" are to be coloured, which ones are dangerous? Nupercaine and 'Amethocaine,' two of the most potent local anæsthetics we possess, are probably no more "dangerous" in clinical use than procaine, if they are administered in the correct dilution and dose, though each of them is many times more poisonous than cocaine weight for weight. A multiplicity of colours would soon defeat its object. Even procaine, usually considered one of the safest local anæsthetics, can be dangerous: on one occasion 1 g. was injected into the subarachnoid space in mistake for 100 mg., because the shape of the ampoule used for the two weights was identical, and the administrator did not read the label. Nothing can prevent mistakes of this sort except knowledge and constant vigilance.

In the operating-theatre, as in the ward, great reliance must inevitably be placed on the skill and vigilance of sisters and their assistants. Errors on their part easily lead to tragedies. For years now there have been occasional deaths owing to confusion between ounces and drachms in doses of paraldehyde.[10] Many ward and theatre sisters are unaware of the possibility of these and the other tragedies mentioned above. Little or nothing is done in some big hospitals to keep theatre sisters up to date with new developments in the drugs and appliances which they handle. How is the theatre sister to know that amethocaine is many times by weight more poisonous than procaine? How is she to know that an injection of 2% nupercaine into the urethra may kill, while 2% nupercaine is permissible in limited amounts as a surface anæsthetic in the pharynx? It would probably be helpful for her and her senior assistant to attend the same lectures which inform the senior medical student and resident (and, dare we say it, perhaps even the junior specialist) of these and similar facts.

PROGRAMME FOR INDIA

THE Bhore Committee's report[11] showed that the general death-rate in British India was about twice, and the infant-mortality rate about four times, that in England and Wales. One of the main causes of ill health was undernutrition: "an ill-balanced and insufficient diet giving only about 1750 calories per day was typical of the diets consumed by millions in India." A further principal cause was shortage of trained personnel. Whereas the United Kingdom had 1 doctor to 1000 of the population, British India had 1 to 6000; and the position with regard to nurses was much worse—1 to 43,000 in India compared with 1 to 300 in the United Kingdom.

These findings were recalled by Sir Bennett Hance, himself a member of the committee, in the Birdwood lecture given to the Royal Society of Arts on Jan. 13. The committee's long-term proposals, he said, called for the division of the Indian subcontinent into a number of population units; each, containing about 3 million people, was eventually to be self-sufficient, training its own medical and ancillary personnel. These main units were to be subdivided into "primary units" with about 20,000 people. The underlying idea was that, except in sparsely populated mountain tracts, no-one should be more than 10 miles from the primary health centre serving the unit. This centre would comprise a 75-bedded hospital with two doctors in charge; in addition there would be four other doctors to undertake preventive work in the villages and homes of the people, and 6 public-health nurses. Aggregations of about thirty such primary centres, covering roughly 600,000 inhabitants, were to be organised from so-called secondary centres. Here would be coördinated the work of the primary units, with whole-time heads of the different medical departments, and a 650-bedded hospital with full provision for the more usual clinical specialties and a laboratory service for the whole area. Here, too, preventive work would be coördinated. At headquarters would be located the main teaching hospital and research organisation, including a medical college with an annual entry of 50 students and a 2500-bedded hospital with full specialist provision. The committee estimated that it would be possible to "produce, within forty years, an integrated preventive and curative National Health Service embracing within its scope institutional and domiciliary provision for health protection of a reasonably high order"; and it advocated meanwhile a short-term programme within the framework of the full scheme. The chief obstacles, said Sir Bennett, were cost and shortage of personnel; and of these the second was the more serious. At present no more than 2200 doctors could be trained each year; on this basis 55,000 might be trained in 25 years, whereas the number required in that time was at least 185,000—all of university standard. The recent constitutional changes, he concluded, might seriously dislocate the time-table of the programme, which he hoped nevertheless to see fulfilled by each of the two new Dominions.

Unhappily the costs arising from partition and the war in Kashmir, together with the loss of revenue through Prohibition, are likely to curtail additional expenditure on social welfare; and for some time to come attention will probably be directed mainly to improving existing medical institutions.

MUCOSAL FRAGMENTS IN GASTRIC JUICE

TEN years ago Hawksley[1] noted that in 10% of 200 patients submitted to aspiration of the resting gastric juice immediately before, and in preparation for, gastroscopy, the samples contained one or more pieces of gastic mucosa, similar to those which Einhorn,[2] in 1894, obtained from the products of gastric lavage. Hawksley—like Einhorn—was convinced that the specimens he obtained were not torn from the stomach wall by suction. In the past two years Hawksley and Cooray[3] have adapted this observation to diagnosis, and have confirmed, that in about one aspiration in ten, fragments of mucosa are obtained. The fragments range in size from a pin's head to a centimetre long. On microscopic study, in all except one, in which carcinomatous tissue was present, the changes of gastritis were observed. The changes are of two main types—those of acute and those of chronic gastritis. In the former, the mucosa is hyperæmic and œdematous, with hæmorrhages in the subepithelial and interglandular tissue. In the latter, the histological changes vary: a large proportion show intense infiltration of the interglandular tissue with plasma cells and lymphocytes; others present evidence of degeneration, atrophy, and faulty regeneration of the epithelium; while a few show aggregations of lymphocytes, giving rise to the appearance of follicle formation—follicular gastritis. In chronic atrophic gastritis cystic changes are not infrequent, and there is often a patchy replacement of the gastric-type mucosa by a mucous membrane of intestinal type—superficial intestinal heterotopia.

The examination of fresh mucosal tags obtained in this way may help to elucidate the problems of gastritis and enable a correlation to be made between symptoms and pathological changes. It will be unfortunate, however, if the desire for specimens of gastric mucosa encourages the inexpert to exert extra suction on his Ryle's tube. The junior nurse or student collecting test-meal specimens does not always treat the stomach lining with the respect

10. *Ibid*, 1947, i, 336.
11. See *Lancet*, 1946, i, 385.

1. Hawksley, J. C. *J. Path. Bact.* 1939, **49**, 585.
2. Einhorn, M. *Med. Rec.* 1894, **45**, 780.
3. Hawksley, J. C., Cooray, G. H. *J. Path. Bact.* 1948, **60**, 333.

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it deserves. When suction is unproductive there is a tendency to pull harder on the plunger, when it ought to be obvious that the eye of the tube is blocked by gastric mucosa sucked into it. The blind method of obtaining biopsy material from the gastric mucosa lately described in these columns [4] is a different matter, for that is not likely to be used except by those engaged in gastric research and who are fully alive to the dangers to which the patient may be subjected by an injudicious suction technique.

RESETTLEMENT

IMPRESSED by shortcomings in our present system of reablement and resettlement, and by its failure to reproduce the successes achieved in the Services during the war, Dr. C. B. Heald (p. 234) puts forward proposals for what he calls "setting-up centres." Patients would go to these centres direct from hospital, and would be of three classes. Some would need only the kind of care provided at a convalescent home; others would require training for a new occupation (e.g., in a Remploy factory); and others again would have to be fitted for work in their own homes. He discusses the conditions necessary for setting up the home-bound successfully, laying emphasis on the need to provide a suitable home.

In considering these constructive proposals it is interesting to have the latest official information on resettlement.[5] Since September, 1946, all employers with more than 20 employees have had to use 3% of disabled persons; and of the 965,000 disabled who have registered since that time about 887,000 were classed as capable of work under ordinary industrial conditions. Of these, some 825,000, or 93%, were in ordinary employment, including those working with smaller firms, or on their own account. Last August there were still 62,079 disabled unemployed, but the work of placing them goes steadily on, and local disablement committees have been asked to study the types of disabled in their areas, and to consider what additional openings might be found for them. It has been decided not to increase the number of "designated" employments—e.g., passenger-lift attendant and car-park attendant—since most of the disabled can hold their own in ordinary industry, if they are enabled to do so. Considerable advances in medical and training facilities have been made, but lack of doctors and medical auxiliaries prevents full use of many of the reablement centres.

Since July 5, 1948, the diagnosis and treatment of tuberculosis has become the responsibility of the regional hospital boards, though the local health authorities are required to make arrangements for prevention, and care and aftercare. One task of these authorities is to guard the patient against relapse caused by a return to unsuitable work; and they have collaborated with the local offices of the Ministry of Labour in finding employment for tuberculous patients who are fit for it. A review made in 1947 at selected local offices, over a period of three months, showed that of 573 cases, 252 were placed in full work, 22 in part-time work, and 3 in sheltered employment. The risk of infection to others makes the placing of these patients difficult and is being further studied. Patients with psychiatric disabilities are also hard to place, and at the moment collaboration between employment exchanges and psychiatric clinics is hampered by the lack of psychiatric social workers. An industrial neurosis unit of 100 beds was opened at Sutton Emergency Hospital, in 1947, for the diagnosis and reablement of neurotic patients with employment difficulties, and serves London and the south-eastern region. During the first year about two-thirds of the 180 patients discharged were placed in jobs; and it is believed that a team of workers such as those at Sutton can do much to settle these men and women in industry.

Reablement of coal-miners has continued at special centres under the auspices of the Miners' Welfare Commission; and the Minister of Fuel and Power has established a national joint pneumoconiosis committee to study this special mining hazard. Work at the Egham Industrial Rehabilitation Centre has continued, and 4321 men have passed through it since it was opened in 1943. Thirteen more such centres are planned, and three of them are already open; all but one will be non-residential. Disablement resettlement officers (D.R.O.s) are now being better trained, and medical interviewing committees have been set up experimentally in some hospitals to interview and examine disabled people, and advise the D.R.O.

THE OMINOUS ARMS CASE

THE Building Research Station of the Department of Scientific and Industrial Research, which recently published a report on Plumbing in America,[1] has arranged to drive home its lesson by showing four American films at the Royal Sanitary Institute's health congress next May. The chief of these films, *The Ominous Arms Case*, is described by F. L. Barrow [2]: it deals with the pollution of drinking-water in buildings by back-siphonage of waste liquids from water-closets, wash-basins, and baths into water-supply pipes. The action takes place mainly in a court-room, where the owner of the Ominous Arms block of apartments, or flats, is being sued by one of his tenants for the illness of her child, alleged to have been caused by plumbing arrangements which permitted this back-siphonage type of pollution. The Building Research Station thinks that this hazard, now widely recognised in America, is not entirely absent in this country, and the codes of practice committee of the Institution of Municipal Engineers evidently shares that view, since it is now considering a revision of the codes which would involve changes in present British Standards and Water Regulations.

Actual medical evidence of illness arising in this way nevertheless remains scanty, and to supply the deficiency Zichis and Piszczek, [3] of Chicago, have made some experiments with the viruses of Western equine encephalomyelitis, St. Louis encephalitis, poliomyelitis (Lansing strain), and lymphocytic choriomeningitis. A plumbing system representing that found in an American two-story residence was constructed for the experiments: the W.C. bowl (of flush-valve type with a side-arm inlet) was placed on a stand 9 feet above the floor, and a sampling tap and drinking-fountain were connected to it at floor level. Virus was added to the water in the W.C. bowl so as to make a 1 in 5000 dilution, and the experiments were carried out at room temperatures which ranged from 24 to 28°C. Half an hour after the virus suspensions had been drawn into the plumbing system by back-siphonage, 100 ml. samples were obtained from both the tap and the drinking-fountain and tested for the presence of virus. Thereafter samples were drawn from the tap at 24-hour intervals to determine how long the virus remained infectious when held in the plumbing system. The investigators conclude not only that such a system can be contaminated with neurotropic viruses but also that the viruses remained infectious for several days when suspended in chlorinated drinking-water and retained in the system at room temperature. They agree

4. Wood, I. J., Doig, R. K., Motteram, R., Hughes, A. *Lancet*, Jan. 1, p. 18.
5. Ministry of Labour and National Service: Second Report of the Standing Committee on the Rehabilitation and Resettlement of Disabled Persons. H.M. Stationery Office. 1949. Pp. 20. 9*d*.

1. See *Lancet*, 1948, ii, 590.
2. *J. Inst. Water Engrs*, 1948, **2**, 486.
3. Zichis, J., Piszczek, E. A. *Science*, 1948, **108**, 503.

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with Kempf and others [4] that the amount of chlorine found in municipal drinking-water is not enough to kill viruses of the neurotropic group.

American observers, however, are not unanimous on the viability of neurotropic viruses in chlorinated water. One point of difference depends on whether pure chlorine or "ammonia chlorine" is used, the latter producing free chlorine and free chloramine, whose combined effect may be greater than that of chlorine alone.[5] Another possible source of discrepancies is the fact that the mouse brain in which suspensions of neurotropic viruses are usually made is capable of absorbing chlorine and may thus protect the virus from destruction by chlorinated water.

THE LIGHT DIET

THE patient on hospital "light diet" is often, either consciously or unconsciously, hungry. His protein reserves need building up; but his appetite is capricious, he is easily put off, and as a rule the food offered him not only looks insipid but is deficient in protein and total calorie value. King Edward's Hospital Fund for London, in a *Food Bulletin* dated December, 1948, say that a really good light diet should contain at least 100 g. of protein; indeed, as much as 300 g. may be needed by some patients in a diet with a total calorie value of 2700. The usual hospital light diet—made up of an occasional egg, a portion of fish or chicken, a helping of milk pudding, watery soups, and synthetic fruit drinks—provides barely half the estimated minimum. The caterer must therefore choose foods with a high protein and calorie content, and present them in an enticing form.

The King's Fund suggest various ways of stepping up the protein content.

Dried milk, which has little distinctive flavour but a protein value of 10 g. per ounce, can be added to a variety of dishes, savoury or sweet. Thus an ounce or two per pint can be mixed with the whole milk used for making puddings, sauces, custards, or moulds; 2 oz. of milk powder can be added to every lb. of flour used in steamed or baked puddings, buns, or cakes; porridge can be made with milk powder and eaten with whole milk, and milk powder can be beaten into mashed potato. This makes it possible to give the whole-milk ration mainly in the form of drinks. Fish, rabbit, and chicken can be steamed or stewed and served with milk sauces, or they can be made into cream moulds with evaporated milk. Tripe, brains, and sweetbreads can be served on toast with thick sauces, while dried egg and grated cheese can reinforce the protein value of many a dish. The recipes proposed in this bulletin should be read after dinner: they are too stimulating to the gastric juices for between-meal reading.

The Fund are emphatic about the fat and sugar rations. Fat is the most concentrated of energy foods, with a calorie value of 218 per ounce. The full ration is only 9 oz. a week, and they insist the whole of it must be used wherever possible. The practice, in many hospitals, of buying less than the full fat ration is not yet dead. Such economy is unjustifiable; the ration is not large, and the whole of it is badly needed, especially by those depleted by disease. Fat can be added to milk puddings, custards, sauces, savouries, and soups, and the proportion of fat to flour in steamed and baked puddings can be increased for those on light diets. The full sugar ration is also needed: even so it is hard to make it go far enough. The importance of colour in the light diet is very great; one glance at an unattractive dish may dam back the gastric flow of a convalescent. The bulletin suggests menus as well as recipes, and will make good reading for any hospital cook who lacks the help of a trained and imaginative dietitian. Even dietitians will find it helpful.

4. Kempf, J. E., Pierce, M. E., Wilson, M. G., Soule, M. H. *J. inf. Dis.* 1945, 76, 120. Kempf, J. E., Soule, M. H. *Proc. Soc. exp. Biol., N.Y.* 1940, 44, 431.
5. Lennen, S. G., Rhian, M., Stebbins, M. R. *Amer. J. publ. Hlth*, 1947, 37, 869.

RENAL BIOPSY IN HYPERTENSION

WHETHER or not the operation of thoracolumbar sympathectomy finds a permanent place in the treatment of hypertension, its present widespread use has made possible the examination of biopsy material from the kidneys of patients with hypertension of varying severity and has therefore provided much valuable information.

In 1943, Castleman and Smithwick [1] reported on such biopsies from 100 hypertensive patients, and they have now analysed the material from 500 patients.[2] This second report was prompted by the criticism that small biopsies from the surface of the kidney were unlikely to be representative of the histological changes in the kidney as a whole. The close similarity of the findings in the two series, the similarity of the grade of renal vascular change in biopsies from both kidneys in a series of 100 patients, and the correlation of these changes with the severity of the clinical picture suggest that this material gives a true picture of renal pathology in hypertension.

In 25% of their cases pathological changes in the vascular system of the kidney were minimal or absent. This is a very different finding from the very high figures for renal arteriosclerosis reported by Moritz and Oldt [3] on post-mortem material from hypertensive patients. Castleman and Smithwick conclude that hypertension often exists in man without any evidence of renal vascular disease or at least without sufficient evidence to explain the elevated blood-pressure. The figures for minimal or absent vascular changes in the kidneys of their patients are unlikely to be equalled in this country, where a more conservative attitude is adopted in the selection of hypertensive patients for operation. Using a modified Keith-Wagener [4] classification of retinal changes, 13% of their patients had papillœdema (grade IV), 24% showed grade-III changes, and 39% had the minimal retinal changes of grades I or O. There was some correlation, especially in the very low and the very high grades, between the severity of renal vascular change and the extent of retinal disease, and there was also a clear relation between the impairment of renal function and the degree of renal vascular change. In their first paper Castleman and Smithwick reported that in 14 biopsies on patients with grade-IV retinitis none showed the changes of necrotising arteriolitis. This emphasises the gap that now exists between the clinician's conception of the malignant phase of hypertension, based largely on the presence of papillœdema, and that of the pathologist who tends still to restrict the term to cases showing typical necrotic arteriolar changes.

Castleman and Smithwick seem to have established that hypertension can exist in man without gross renal pathology. This is in accord with the view that widespread arteriolar spasm precedes organic vascular change in hypertension and with the findings of Goldring and colleagues,[5] who, using the inulin and diodrast clearance technique, reported that the earliest functional change in the kidneys of hypertensive patients appeared to be a reversible spasm of the efferent glomerular arteriole. Those who follow Goldblatt [6] in maintaining that renal ischæmia is the underlying cause of essential hypertension must apparently look elsewhere than the renal arterioles for a primary pathological lesion.

1. Castleman, B., Smithwick, R. H. *J. Amer. med. Ass.* 1943, 121, 1256.
2. Castleman, B., Smithwick, R. H. *New Engl. J. Med.* 1948, 239, 729.
3. Moritz, A. R., Oldt, M. R. *Amer. J. Path.* 1937, 13, 679.
4. Wagener, H. P., Keith, N. M. *Medicine*, 1939, 18, 317.
5. Goldring, W., Chasis, H., Ranges, H. A., Smith, H. W. *J. clin. Invest.* 1941, 20, 637.
6. Goldblatt, H. *Physiol. Rev.* 1947, 27, 120.

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STANDING ADVISORY COMMITTEES

THE Minister of Health has made a statutory order constituting nine standing advisory committees which will advise the Minister and the Central Health Services Council. The members of the committees are appointed for a term of 1, 2, 3, or 4 years, or while holding other official appointments. Those shown under (*a*) have been appointed by the Minister after consultation with the Central Health Services Council; those under (*b*) have been appointed after consultation with representative organisations.

MEDICAL COMMITTEE

(*a*) Miss Janet Aitken, F.R.C.P., Prof. W. G. Barnard, F.R.C.P., Aleck W. Bourne, F.R.C.O.G., J. A. Brown, M.D., Sir Ernest Rock Carling, F.R.C.S., Sir Henry Cohen, F.R.C.P., H. Guy Dain, F.R.C.S., Sir Allen Daley, F.R.C.P., Sir William Gilliatt, F.R.C.O.G., E. A. Gregg, L.R.C.P.I., W. V. Howells, M.B., Horace Joules, F.R.C.P., Prof. A. J. Lewis, F.R.C.P., W. G. Masefield, M.R.C.S., Lord Moran, P.R.C.P., W. N. Pickles, M.R.C.P., Sir Harry Platt, F.R.C.S., Prof. J. C. Spence, F.R.C.P., C. W. Walker, M.B., Lord Webb-Johnson, P.R.C.S.

(*b*) W. Russell Brain, F.R.C.P., Somerville Hastings, F.R.C.S., R. L. Newell, F.R.C.S., Wyndham Parker, M.B., J. Ralston Paterson, F.R.C.S., W. G. Patterson, M.R.C.P.

Secretary: Mr. D. Emery (Whitehall 4300, extension 172).

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(*b*) Prof. Harry Berry, B.SC., J. O. Davidson, M.P.S., Paul Dobson, M.P.S., P. J. Gibbons, M.B., John Gilmour, M.P.S., C. H. Hampshire, M.B., J. C. Hanbury, J. B. Hough, M.P.S., H. N. Linstead, PH.C., M.P., G. A. Mallinson, M.P.S., D. E. Sparshott, M.P.S., Prof. E. J. Wayne, F.R.C.P.

Secretary: Mr. F. F. Marchbank (Victoria 8540, extension 353).

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Secretary: Mr. H. J. Clarke (Kensington 3456, extension 5).

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(*b*) H. E. A. Boldero, F.R.C.P., Prof. E. C. Dodds, F.R.C.P., F.R.S., Prof. Ernest Finch, F.R.C.S., K. I. Julian, Prof. Hilda N. Lloyd, F.R.C.O.G., Prof. W. V. Mayneord, D.SC., Prof. J. S. Mitchell, M.B., V. E. Negus, F.R.C.S., J. Ralston Paterson, F.F.R., J. A. Stallworthy, F.R.C.S., Prof. Matthew Stewart, F.R.C.P., C. J. L. Thurgar, F.R.C.S., Prof. R. Milnes Walker, F.R.C.S., Prof. B. W. Windeyer, F.F.R.

Secretary: Mr. R. Gedling (Whitehall 4300, extension 253).

* Invitation to serve not yet accepted.

DISCUSSIONS AND DECISIONS

FINAL decisions about the terms and conditions of service of hospital staffs have been again deferred. The provisional proposals of the Ministry of Health are under discussion with the Joint Committee of Consultants and Specialists, which is advising the Ministry about their possible modification. When this confidential review is complete, the Ministry will issue its proposals publicly and they will have to be considered by the committee's constituent bodies. To allow time for this, the present interim arrangements will have to be continued for a further three months. Though now inevitable, this delay will undoubtedly cause hardship to a substantial number of the younger doctors, including ex-Servicemen, who are working whole time at remuneration well below what they had reason to expect after April 1. We hope that every effort will be made to meet their difficulties so far as this can be done. For too many the period of uncertainty has already lasted too long and the fact that the final terms will be retrospective will not help those who have not pet secured appropriate posts.

The Joint Committee of Consultants and Specialists has Sir Lionel Whitby as its chairman, and is made up of the following representatives:

Royal College of Physicians.—Lord MORAN, Prof. W. G. BARNARD, Dr. H. E. A. BOLDERO.

Royal College of Surgeons.—Lord WEBB-JOHNSON, Mr. E. F. FINCH, Mr. MCNEILL LOVE.

Royal College of Obstetricians and Gynæcologists.—Sir WILLIAM GILLIATT (deputy chairman), Mr. H. J. MALKIN.

Royal College of Physicians of Edinburgh.—Dr. J. D. S. CAMERON.

Royal College of Surgeons of Edinburgh.—Sir HENRY WADE.

Royal Faculty of Physicians and Surgeons of Glasgow.—Dr. W. R. SNODGRASS.

Consultants and Specialists Committee established by the B.M.A.—Dr. T. ROWLAND HILL, Dr. C. E. KINDERSLEY, Mr. W. S. MACK, Mr. A. M. A. MOORE, Mr. R. L. NEWELL, Mr. T. HOLMES SELLORS.

The Negotiating Committee having been disbanded, discussions with the Ministry on general practice are being conducted with the General Medical Services Committee, which will report to a special conference of local medical committees on March 3. Remuneration will also be considered at a special representative meeting of the British Medical Association on March 29.

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Special Articles

SETTING UP THE DISABLED*

C. B. HEALD
C.B.E., M.D. Camb., F.R.C.P., D.P.H.
CONSULTING PHYSICIAN TO ROYAL FREE HOSPITAL

MORE and more attention is nowadays being paid to the fate of the patient after he leaves hospital.

Every investigation brings a similar group of facts to light. First, a high relapse-rate entails waste of beds, effort, and money, and the causes of relapse therefore deserve more thought. Secondly, the task of setting up the disabled, like the approach to positive health, is a study in itself. Thirdly, of the various groups into which the disabled fall, the home-bound are the least provided for and the most difficult to re-establish.

I have chosen the term "setting up" deliberately. The dictionary defines the setter-up as "one who establishes"—implying a positive act, by a new or definite process. This is an improvement on words beginning with "re"—rehabilitation, re-employment, reinstatement—since these all signify a return to some former state. We should get away from the idea that the disabled should always, or whenever possible, be pushed back to their former employment. Such reinstatement suits some, but only some.

PRESENT WEAKNESSES

In the British Legion unit of rheumatology we found the causes of relapse often went back to the patient's time in hospital under the unit. Occupational therapy had been haphazard, or had no real relation to the patient's ability, make-up, or home conditions. The occupational therapist had not been trained in commercial methods, and knew nothing of marketing, or of possible openings. From the patient's point of view, the lack of any incentive—such as payment, or a safe selling organisation for completed work—made this side of our treatment unreal and largely useless. Relapses after the patient had left the unit were due to such factors as delay in finding suitable work, or a forced attempt to return to former employment—in short, to disuse or overuse of the affected joints. Housing, family troubles, financial difficulties, and the weaknesses in the system worked by disablement resettlement officers have all played their part.

The difficulties of reinstating an arthritic who is only fit for work at home are great: he has trouble in getting out of bed, dressing, feeding himself, travelling to work, and doing anything he has to do, right up to bed-time. Any additional hurry or strain may be enough to start a relapse.

Bodies to help the disabled, and openings for the disabled, are multiplying fast. Among these may be mentioned the Government Remploy factories, and village settlement schemes such as Papworth. The Lord Roberts Memorial workshops have done pioneer work and offer a wide range of help to cases coming under their care—far wider than that permitted by the Disabled Persons Act.

THE HOME-BOUND

The village settlement is the method of choice for tuberculous or infectious patients. The Remploy factories will in time cater for the ambulant or semi-ambulant, though some will never be able to fit in with this scheme—for example, the fully ambulant living deep in the country. It is the home-bound patients, including most quiescent arthritics, chronic chest and heart cases, and epileptics that present the greatest difficulties.

Housing is the first of these. House anxiety, overcrowding, and unsuitable housing are potent factors in relapse, and are closely linked with malnutrition. The site of the patient's home—whether in a town or up a lonely Welsh valley—his family ties and tensions, the earnings of his immediate relatives, and his aptitude and application, must all be taken into account before any attempt is made to set him up. Among these, however, the house is paramount, being as important to the patient as its shell to a snail. It is his workshop, and his life is governed by it.

A WORKING PLAN

It is often said that people do not mind being separated from their homes if it means they will get preferential treatment for their disease or disability; but that when it comes to training for work, they dislike being transferred to some distant centre for the purpose, even if suitable permanent work is promised when training is complete. But I am assured by the works manager of the Queen Elizabeth Training Centre at Leatherhead, that this is only partly true, and that if transfer meant suitable or improved living accommodation 90% would not hesitate to transfer for training.

To train the home-bound in their own homes would be as unsatisfactory as to train doctors by a correspondence course; nor would it settle their problem to collect them and take them to Remploy factories, and return them home at night, even if this were a practical proposition.

As things stand in the National Health Service, general hospitals, and especially the teaching hospitals, seldom have anywhere to send long-term cases, and are loth to accept them because they block acute beds. A bottleneck has thus been created.

I suggest that as a pilot experiment, a setting-up centre, staffed by specialists, should be established. Three classes of patients would go there straight from hospital: those who could be expected to return to their former work in 3–6 weeks (the convalescent-home type of patient); patients who would be expected to stay longer, and who would probably need work different from what they were doing formerly (the future Remploy factory workers); and the prospective home-bound. The centre would therefore need a convalescent section, a hostel or hardening-off section, and a section for training the home-bound. A general physical-medicine department would be needed, as well as an educational and an industrial psychology section, all of which would keep in close touch with the parent general hospital or hospitals. The gap between hospital treatment and return to employment could thus be bridged, the risks of relapse diminished, the time of disablement reduced, and the general hospital waiting-lists relieved. All this was successfully done during the war in the Royal Air Force medical rehabilitation units.

It is useless to train a home-bound person for a craft which he will have no scope to exercise when he gets home. The scheme must provide his equipment and materials, guarantee him access to a market, and ensure that when he sets up work in his home he will get union piece-rates. Above all it must guarantee him a home that he can use as his factory. In the village settlement the patient moves from hospital to sanatorium and hostel, and finally to his permanent cottage on the site near the works. In the scheme suggested here the centre would watch over a cottage settlement of a different type—a settlement of widely dispersed cottages, each planted where conditions were favourable. Prefabricated houses might be bought and placed in areas where home work could be absorbed, and in the neighbourhood of Remploy factories from which the work could be supervised.

CONCLUSION

Setting up calls for a skilled study of the individual—his history, neighbourhood, aptitudes, and character,

* From a paper read before the Heberden Society on Dec. 3, 1948.

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but above all his home. He must be freed from the notion that he must work back painfully and inefficiently to a former state; instead he must be established, enlivened, and given security. Setting up is a special phase in his life, distinct from wellness or active illness. Properly used it should reduce the relapse-rate, ensure better coördination between responsible bodies, provide continuous care for the patient, speed the turnover in general hospitals, and encourage the pooling of special knowledge. If we pay more attention to the home we shall go far towards solving the problem of the home-bound.

TERMS OF SERVICE

DR. HILL'S REVIEW

ADDRESSING the Metropolitan counties branch of the British Medical Association on Jan. 27, Dr. CHARLES HILL, the association's secretary, said that negotiations on remuneration had been and would continue to be based on the two Spens reports. As regards the specialists' report, the Minister had circulated confidentially his own first interpretation; and the joint committee representing specialists and consultants was advising on changes which seemed desirable to make this interpretation more acceptable. The next stage would be the publication, in a few weeks, of the Minister's proposals. This procedure, with opportunity for examination and comment, took time; and it would involve the extension for a further 3 months of the provisional terms. The final terms would apply retrospectively; and meanwhile discussions were "progressing hopefully." The Spens reports would have their relevance also to the salaries of public-health medical officers; and the association was determined to have the remuneration of these officers examined without further delay by the Whitley council.[1]

Turning to general practice, Dr. Hill said that the difficulty here centred on the amount of betterment. Two factors had to be considered: (1) the changed value of money; and (2) increases in remuneration secured by other professions. At the end of 1946 the Government had fixed betterment at 20%—a percentage to which it still adhered. Expert opinion set the middle-class family budget in 1945 at 145% of pre-war; and now it was set at 185%. The Minister had agreed that the question of betterment should be referred to the appropriate Whitley council when this was set up. Only when suitable betterment had been secured would it be time to see whether the Spens report was being properly applied. Meanwhile a limited survey had shown that, on the basis of 20% betterment, the committee's recommendations had for the most part been satisfied in the upper and middle ranges of income; in the lower-income groups remuneration possibly fell sometimes below the recommended scales. All practitioners now had difficulty in knowing where they stood. There had been a certain amount of redistribution among practices, and some individuals and groups were suffering very considerable hardship.

Discussing the increased burden of work, Dr. Hill pointed out that a complaint of overwork automatically raised the question of reducing the size of lists. With reduction of lists and the related increase in capitation fees which would be necessary, remuneration would tend to be equalised; and it might then be found that more than the 10% (aged 40–50) proposed in the Spens report were earning incomes in advance of their colleagues. The order of approach should be: (1) improvement of betterment; (2) review in relation to the Spens report; and (3) reduction of the maximum list below 4000 if it was agreed that the work was excessive.

1. See *Lancet*, Jan. 29, p. 195.

The most pressing problem at the present time was that of practitioners with small lists. In the case of rural practitioners substantial relief had been afforded by the recent increase in the mileage fund. Of this increase £500,000 was new money; "we have broken through the suggestion that every increase in mileage would have to come from remuneration." With regard to those in overdoctored areas, the association had held that the capitation fee would influence practitioners so much that no control would be needed, and yet it was no use telling these men and women that they were part of the movement of doctors; they should not be uprooted. A proper livelihood had to be secured for practitioners with 1500–2000 patients on their lists. This could be achieved in either of two ways: (1) by a basic salary, affording an "expenses amount" for small practices, in which the expenses were relatively greater; or (2) by a tapering capitation fee.

CONTROL OF NARCOTIC DRUGS

FROM A CORRESPONDENT

CULTIVATION of the poppy as a source of opium was fully established by the middle of the 15th century. The initial Chinese practice of taking opium medicinally changed after a time into one of smoking it. This new phase was associated with the introduction of tobacco-smoking from the Philippines. And tobacco proved a lesser evil than the early Chinese reformers expected, while opium-smoking proved a far greater danger than they feared.

Opium from Malwa, Central India, was originally exported to China by the Arabs, the Portuguese, and the Dutch. From 1699 onwards the East India Company had a monopoly of the English trade with China, and "outside" merchants could trade only under its licence. This monopoly was not abolished until 1834. The English traders shipped to China raw cotton, opium, and woollen goods in exchange for tea, silk, and cotton cloth. In 1773 Warren Hastings introduced a government monopoly for opium manufacture and export. Bihar, as the principal region of poppy cultivation, and Patna, as the centre of opium manufacture, prospered greatly. In 1783 Hastings wrote of opium as "a pernicious article of luxury which ought not to be permitted but for the purpose of foreign commerce." The excise on opium had been regarded by the later Mogul emperors as a subject for State monopoly. Under the fiscal system which the East India Company, and later the Crown, inherited from their predecessors, opium revenue ranked next in importance to that derived from land. It came from the profits of the State monopoly of the sale of the drug to China and other countries, and that sold locally. In 1881 the Indian opium revenue yielded 780 million rupees.

When in 1800 the Chinese government showed itself resolved to suppress the traffic in opium, the trade reverted to private traders. In 1839 Commissioner Lin Tse-Su was appointed by Emperor Tao Kaung to eradicate the opium habit of his subjects at all costs. The surrender of all chests of opium in the hands of the British was agreed to under pressure by Captain Elliot, chief superintendent of trade in China. After a dispute on this issue British ships were prohibited from entering Cantonese waters. In an affray at Hong-Kong on July 7, 1839, a Chinese was killed by a party of British sailors. The British authorities were unable to lay hands on the culprit or culprits and hand them over to the Chinese. This was the immediate cause of the "opium war." The convention at Nanking was concluded in 1842, and China paid Britain an indemnity of 21 million Chinese dollars. After 1855 not only was cultivation of the poppy in China permitted but import of opium from India was legalised. Trade in opium reached its peak

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during the latter part of the century. In 1906 a competent Chinese authority estimated that 27% of adult males in China smoked opium. In the following year China was reckoned to have consumed 600,000 chests of opium (one chest = 140 lb.), of which she produced 360,000 herself and imported 51,000 from India.

Since foreign traders were to no small degree responsible for fostering this pernicious traffic, China felt compelled to enlist the aid of foreign powers to suppress the opium evil. In 1907 she entered into a ten years' agreement with India under which the latter agreed to reduce the amount of opium exported to China by 10% annually, provided there was a corresponding decrease in production by China, and in imports from Persia and Turkey. By 1910 it was clear that China was, to a substantial extent, carrying out her part of the bargain, and India decided to discontinue further opium shipments to China in 1913, four years before the stipulated time. According to Sir John Jordan's statement at the Opium Advisory Committee's meeting in 1917, "China had almost freed herself from the curse of poppy." But political troubles, coupled with the lack of a strong, stable, and honest central government, put a stop to this desirable consummation, though those in authority were doing their best to root out the evil. To lessen the danger of opium smuggling into China the Indian government agreed to confine the remainder of opium shipments to legitimate demands of non-Chinese markets. Thus on her own initiative India's opium exports to destinations other than China were subjected to successive restraining agreements with the countries concerned. The financial sacrifices incurred by India to help China reform herself amounted to several million pounds a year. Indian revenue from opium dropped from 780 million rupees in 1881 to 490 million in 1939–40. The area under poppy in British India was progressively reduced from 586,000 acres in 1901 to 37,012 acres in 1931–32, and Indian shipments of opium in 1934–35 totalled only 663 chests compared with 51,000 chests to China alone in 1907.

INTERNATIONAL CONVENTIONS

As is well known, after the first world war large quantities of surplus drugs found their way into illicit channels, and thousands of people, especially in the defeated countries, became addicts. No country was able to protect itself single-handed against the drug evil, and the traffickers were able to direct illicit trade in countries other than those in which they were domiciled. In 1920 one country alone had as much morphine, cocaine, and heroin as the entire world needed for legitimate purposes.

The Geneva Convention of 1925 was worked out by the League of Nations to combat this peril. It instituted a system of import and export certificates, under which narcotic drugs could not be exported without the express authority of the governments concerned, and all shipments not covered by such certificates were deemed illegal and liable to seizure.

Indeed, even earlier, in 1923, India had introduced a certificate system whereby all exports must be covered by certificates from the government of the importing country that the consignment was approved and was required for legitimate purposes. Exports to Singapore, Saigon, Batavia, and Macao thus continued. The entire amount was shipped under the system of direct sales to foreign and Colonial governments, the system of auction sales in Calcutta to traders for export for foreign countries being terminated in 1926. India later decided to reduce her shipments of opium to Far Eastern countries for other than medical and scientific purposes by 10% yearly so as to extinguish them altogether by the end of 1935. No Indian opium is shipped to America or any European country except Great Britain, where it comes under the operation of the Dangerous Drugs Act. Measures controlling consumption in Britain of a range of dangerous drugs were strengthened by regulations which came into force on Jan. 1, 1949.

Provisions of article 6 of the Hague Convention of 1912, to which more than sixty countries were parties, had called for the gradual suppression of the manufacture, international traffic in, and use of, prepared opium. At the Geneva conference in 1924–25 the United States delegation sought to put an end to opium-smoking by confining production of the drug to purely medicinal and scientific requirements. This was the goal of every government represented, but in view of formidable practical obstacles the path of regulation and restriction leading to eventual prohibition was generally favoured. For one thing, the rival Chinese war lords, desperately needing revenue, did not hesitate to increase the area under poppy. For another, poppy-growing Persians were opposed to restriction unless the United States and others favouring such a step were prepared to finance a substitute form of agriculture. Moreover, the governments of Malaya and Hong-Kong, deriving substantial revenues from opium monopoly, were reluctant to forgo them at one stroke before other financial arrangements could be devised and put into force. These considerations prompted Great Britain and certain other like-minded governments to dissent from the American proposals, and the United States and China representatives withdrew from the conference.

Of the world production of 18,504 tons of raw opium during the four years 1934–37, China was credited with 65·4%, India 6·7%, and Turkey 6·1%. The pamphlet on Pre-war Production and Distribution of Narcotic Drugs, giving those figures, also states that "Chinese opium has never appeared in licit international traffic. It is likely that all or almost all the opium was used for domestic consumption by addicts." In the early '30s the Chinese government took active steps against opium production and smoking. It was determined to counteract the sinister fostering of the drug habit in China by Japan, whose army became the protector and exploiter of the old and new opium dens in occupied territory—because the Chinese addict was less prone to "dangerous thoughts," and fortunes could easily be made out of the traffic.

Of the total world output, 970 tons of raw opium was exported to countries manufacturing morphine, and 782 tons to territories making "prepared opium" for smoking. Morphine manufactured during the same four-year period was computed at 137,360 kg., of which 22% was attributed to the United States, 16·3% to Germany, 11·1% to Japan, and 5·8% to Great Britain. Normal annual licit world needs for these drugs are given as 8355 kg. for morphine, 950 kg. for heroin, and 3840 kg. for cocaine.

RECENT YEARS

Meeting in London in the spring of 1944, under the presidency of Sir Atul Chatterjee, the Permanent Central Opium Board reviewed the information available, and control measures over the trade and manufacture of narcotic drugs for countries already, or about to be, liberated. Three years earlier the government of China had prohibited the use of opium for smoking in that country. Late in 1943 the British and Dutch authorities had decided to ban the use of opium in their Far Eastern possessions on their liberation. In February, 1944, Senator R. V. Keane, Australian minister for transport and customs, had announced that the smoking and production of opium would be suppressed in all Commonwealth territories recaptured from Japan.

The Judd resolution, passed unanimously by the U.S. House of Representatives and the Senate, and approved by the President, is in line with the long-

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standing opium policy of that pragmatical nation. It is a public announcement of the conviction of the Congress that the second world war ought not to be an occasion for permitting expansion and spreading of illicit traffic in opium, but rather an opportunity for eliminating it. The U.S. State Department is resolved to secure the coöperation of opium-producing countries in the solution of this world problem. Both the Burmese and Chinese governments are coöperating to put down illicit traffic in opium. Turkey is redoubling her efforts to check illicit shipments. A Bill before the Iranian parliament prescribes the death penalty for anyone found smoking opium. Another enactment under consideration proposes to prohibit poppy cultivation in Iran despite the financial sacrifice such a step entails. Afghanistan, too, is taking measures to suppress the narcotic traffic and addiction inside that country. In October, 1945, an order from General MacArthur's headquarters told the Japanese to curtail cultivation of opium poppy, coca leaf, or hemp from which narcotic drugs are made; it demanded the destruction of such standing crops and "freezing" of all existing stocks, and warned the Japanese that no imports of narcotics would be permitted except with specific Allied consent. In the New World, Mexican authorities are redoubling their efforts to suppress clandestine poppy cultivation, and are joining with the United States in suppressing opium smuggling into the latter country.

In 1946 the United Nations Narcotics Commission was organised as an integral part of the Economic and Social Council. It took over the control activities carried out with commendable success by the Opium Advisory Council of the League of Nations. Also, the work of the semi-autonomous Permanent Central Opium Board was incorporated with that of the U.N. Council. Before the war an average of 127 reports were received each year, 44 from sovereign States and 83 from other territories. In 1945 the total declined to 69 (29 from sovereign and 40 from other territories). The Narcotics Commission has requested the Economic and Social Council to remind member governments of their obligation to send full annual reports promptly. Although a party to the 1925 and 1931 conventions, Spain has failed to furnish statistics, and has persistently imported drugs above her legitimate needs.

During the war Germany produced nearly all her morphine from poppy straw, and poppy cultivation spread throughout Germany; but it is being put down by the occupation authorities. Russia has controlled her narcotics traffic satisfactorily.

THE DRUG TRAFFIC TODAY

Crude opium and smoking opium still maintain their important relative position in illicit traffic, the principal sources of supply being Mexico, Iran, and India. Last October the Australian customs authorities announced the seizure of 350 lb. of opium worth £22,400, aboard the motor-ship *Chanda*, and last year the Egyptian customs authorities seized 8 tons of narcotic drugs.

The Economic and Social Council recently endorsed the recommendations of the Narcotic Drugs Commission. A draft convention is being prepared so as to simplify international control and include the newly developed synthetics, such as 'Amidone,' not covered by the convention of 1931. Meanwhile the council has recommended that the system of reporting on illicit drug traffic should be tightened up, that scientific methods should be used to ascertain the territorial origin of raw opium, and that steps should be taken to suppress opium-smoking in the Far East. Also it is going to convene a conference of all producing countries in the hope of curtailing production and shipments of drugs.

The Permanent Central Opium Board, with its membership reconstituted by the U.N. Economic and Social Council, derives its authority from the Geneva Convention of 1925, and receives annual returns from each contracting party to the conventions of 1925 and 1931. It has before it statistics on narcotic drugs from every country for the previous year, and also the last annual statement on world requirements, country by country, issued by the Supervisory Body.

The first post-war report of the board, dealing with the legitimate manufacture and distribution of drugs derived from the opium poppy and the coca leaf, records that the legitimate production of nearly all drugs is now much greater than is justified by medical and scientific demands. Past experience has shown that the presence of large amounts in licit trade usually precedes a growth in addiction and the expansion of illicit demand and supply. There is fascination for the weak-willed in drugs, and money for the unscrupulous in their traffic.

The report reveals the disturbing rise in consumption of heroin, whose power and swiftness to occasion addiction is generally acknowledged, and names Finland, Italy, Sweden, Australia, and New Zealand as excessive users of the drug. Finland's heroin consumption trebled between 1936 and 1946, amounting in the latter year to over 25 kg. per million inhabitants, and estimates by the Finnish government for 1949 are even higher—namely 51 kg. Sweden doubled her heroin requirement during the same period, whereas, curiously enough, her neighbours Norway and Denmark have virtually abandoned its use. Italy has stepped up her consumption by 50 per cent. since 1936. Between them Finland and Italy consumed over half the total world production of heroin in 1947. Among countries of the British Commonwealth, Australia and New Zealand used as much heroin per capita as the United Kingdom and Canada in the same year, and in the latter country consumption had risen fivefold between 1936 and 1946. The situation in Germany, the report points out, is fraught with danger. For one thing, before the war she was one of the largest manufacturers of narcotic drugs and, favoured by her geographical position, one of the major centres of illicit traffic; for another, with the breakdown of the four-power administration, central supervision and control has become extremely difficult. Of late several medically advanced countries have done without heroin, "a fact," opines the Board, "which alone is sufficient to show that there is an a priori case for its total abolition." The expert committee's recommendations, on either abolishing or curtailing heroin's use, now that there are efficient and relatively harmless substitutes, will be awaited with interest.

In dealing with matters of common concern the Permanent Central Opium Board coöperates with the Drug Supervisory Body of the United Nations, which is more closely connected with illicit traffic matters. Its report is now before W.H.O., under whose auspices an expert committee on habit-forming drugs met for the first time in Geneva on Jan. 24.

CONCLUSION

To sum up, 37 years ago article 6 of the Hague Convention called for the suppression of the manufacture, international traffic in, and use of prepared opium. Following recent vital decisions of the Indian, Chinese, British Colonial, Dutch, and Australian authorities these aims can now be fulfilled. But to enforce suppression of the traffic in narcotics, and the policy of total prohibition, will call for far more drastic restriction of the area of crops from which narcotic drugs are prepared in growing countries, and for coöperation between exporters of the drugs and those who import them for bona-fide scientific and medical uses.

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In England Now

A Running Commentary by Peripatetic Correspondents

VISITORS to our laboratories may be V.I.P.s, scientists, or coots (strictly speaking, of course, a great many V.I.P.s are coots). The menace of the V.I.P. has already been dealt with (*Lancet*, 1947, i, 647). Scientists who visit us are of two classes: (1) those who are working in one's own field, and (2) the others. Class 1 scientists, provided they are not spies from spiv laboratories, are a joy to meet and are welcomed with open arms. Class 2 scientists are usually dealt with by five-minute demonstrations of slides or graphs, and a reprint or two may even change hands. Coots are a menace of the first magnitude. There are various ways of dealing with them, but the basic technique is "passing the coot," and the speed with which coots are passed from laboratory to laboratory is quite remarkable. The library is a favourite funk-hole when coots are about, although one biochemist speaks highly of a W.C. in the basement and yet another favours a round of golf. One worker thought he had solved the problem. "Are you scientists?" he used to ask visitors who looked like coots. A negative answer resulted in an immediate slam of the lab. door and the sound of a key grating in the lock. However, one day he popped the question to a small crowd of sightseers, and, receiving an answer of "yes," talked freely and fully about his work for nearly an hour. We could almost hear the vegetations on his heart valves crumbling when we told him afterwards that his visitors were Christian Scientists. Nowadays he will only talk to approved scientists, and on all other occasions he joins the biochemist in the basement.

* * *

I doubt whether many Peripatetics going about their legal ways have had to spend a night in the hospital on Ellis Isle as official guests of the U.S. Immigration Authorities. With 14 other "detainees," I was taken there on my arrival in New York because my papers were not in order. Several small wiry men, with poker faces beneath their wide hats and guns in hip pockets, packed us into cabs, locked the doors, and drove us in convoy from the Piers downtown to the ferry station. Here we were made to wait a long time before being shepherded, after constant recounting, on to the ferry boat.

Conversation with our janitors was limited, their only facial movements being the transference of gum from one cheek to the other, while my companions, mostly D.P.s, potential G.I. brides whose husbands had carelessly forgotten to put up the necessary bonds, and one frank stowaway, apparently accustomed to such formalities, slept or discussed the situation philosophically, usually in German. The ferry boat made its fussy way to Ellis Isle, appropriately situated behind the back of the Statue of Liberty, all gloriously illuminated. We were counted again, checked over, and herded off the ferry, and as we passed the empty wire cage of the internment camp, with its sinister guard-boxes, there were numerous comments, mostly derogatory, from the D.P.s, connoisseurs of such structures. After traversing innumerable long dark corridors, we were left, with guards, in a waiting-room labelled "visitors." This was not quite so ironical as it first seemed, because the rows of chairs turned to the glass windows were for those "detainees" who might be lucky enough to have a visitor to converse with across the dividing wall.

Not being particularly impressed with the dormitory arrangements, I declared I was a "medical," and as a result was hastily transferred to the hospital on the other side of the island. It was now 2 A.M., yet the nursing-staff welcomed me with "crackers" and milk, and were frankly incredulous at having an English doctor "detainee" for the night. I was flattered to find I had made such a welcome break in their usual run of drunken seamen, "malarias," and similar unfortunates. My large cubicle was well equipped but had two rather depressing oleographs on the wall, one of snow, the other of high summer, both in landscapes that were obviously not America. The night was full of noises: bell buoys clanging in the fog and a police siren wailing (this had been going when we arrived at the ferry station and its eerie wail could still be heard at 3 A.M.). Fog swirled in through the window and altogether Ellis Isle was a most foreboding place.

No early morning cup of tea, but a cup of milk, followed by vast quantities of iced water. Then came breakfast in the best American style: hot cereal, eggs, bacon, fried potatoes, toast, and of course coffee plus, plus. This was regulation diet: how large a supplemented meal must be I cannot imagine. Nurses and doctors, viewing me as a strange wonder, came to call, and the morning passed very pleasantly discussing all aspects of medicine from the shortage of nurses to the difference between "appendicectomy" and "appendectomy," while the "high-ups" were straightening out this small matter of my irregular entry to the United States. One ward in this hospital was devoted to seamen of all nationalities who had contracted pulmonary tuberculosis. They had all received streptomycin, apparently in unlimited quantities, and it was with mixed feelings that I watched men receiving this "therapy" ask for day passes to visit New York.

Once my papers were found to be in order I imagined I would be released, but I was quickly and sadly disillusioned. No "detainee" on Ellis Isle is allowed to go anywhere without a guard, either policeman or warden, who has to announce by telephone his forthcoming arrival to the man ahead. When he is reached the guard hands over his charge and signs for him as for a registered parcel. Whatever the unfortunate charge may feel about all this, he is powerless to speed up or avoid the process, and so I was passed from guard to guard, post to post, delivered and signed for innumerable times while I went in search of my baggage and valuables. Hours went by, and eventually I was joined by a Spanish woman and her three children who could not speak a word of American. Her warden informed me we might have to spend another two nights on Ellis Isle because the next day was a public holiday, and the ferry would not run. This idea was so unpleasant that, becoming desperate, I used a certain amount of unseemly language on my jailers. The effect was magnificent: mouths would have gaped open but for the well-chewed gum. Within ten minutes we were all on the ferry again—but still under escort. When I was eventually delivered a free man on the sidewalks of New York, two men dashed by, followed by a number of policemen, who were doubtless counting the fugitives as they took sporadic shots at them.

* * *

If "there is and can be no science . . . divorced from politics" (Waddington [1]), I suppose that Medica really is married to that man after all. Well, all I can say is the poor girl ought to get a separation. Why, last year the brute only gave her about £70,000 for herself, while he simply squandered money on those sisters of hers. Do you know he spent about £50 million on that spiteful cat Milly Science who's in the A.T.S., and even that dowdy creature who works in a factory got about £15 million (Enogat [2]). Poor Medica could scarcely be worse off if she was an unmarried mother like Necessity who had that clever child and nobody ever knew who the father was.

* * *

MY GARGLE

A gargle is a lovesome thing? What rot!
Cold, hot,
Warm, cool,
It's not.
The veriest fool
Must be that fellow who'll
Contend that he has got
Ease for a throat that's aching somethink crool
By laving same in brine.
I'm bloodsome sure it's not eased mine.

1. Waddington, P. J. *Lancet*, Jan. 1, p. 41.
2. Enogat, J. *Science News*, 1947, 5, 98.

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Letters to the Editor

LIVER EXTRACTS

SIR,—I am glad that Dr. McSorley (Jan. 22) has raised again the question of the dosage of liver extracts in the treatment of pernicious anæmia. I dealt with this matter at the Royal College of Physicians in March last year in my Oliver-Sharpey lectures, which are to be published in the near future.[1]

Adequate dosage of liver extract depends on several factors, but in particular on the degree of anæmia, the presence of complications, and the hæmopoietic potency or strength of the liver extract used. I have constantly stressed that full and adequate dosage must be given and maintained from the initial treatment until the blood-count is normal, and until any subacute combined degeneration has improved considerably (although in these latter cases desiccated hog's stomach has proved much more valuable). According to the type and make of liver extract used, the initial dosage will vary from 2 ml. daily to 4 ml. twice or thrice weekly, with subsequent reduction to maintenance levels of 2–4 ml. weekly or fortnightly; I do not now recommend intervals longer than two weeks between individual doses.

These doses are distinctly greater than the pre-war ones for several important reasons. Many batches of commercial liver extract supplied for use in treatment cannot have been properly and individually tested clinically before issue. I have referred to this many times in the past,[1 2] for in my clinic, as also no doubt in others, I see from time to time patients with quite uncomplicated pernicious anæmia who have failed to respond to massive doses of "liver extract." They usually appear in groups of perhaps 2 or 3 over a short period, according to the particular batch of inactive liver extract being supplied at the time in the area. This is much more likely to occur with the highly purified liver preparations. It is not sufficient for manufacturers to assume that because one liver batch is active the next one will be so, even when apparently the same conditions of preparation have been employed; every one must be tested, or else bulked with others and so tested in larger batches.

From the early days of the war up to the present time another startling factor has operated. Pre-war liver extracts for the treatment of pernicious anæmia were made from fresh or frozen, but *healthy*, animal livers, and the manufacturer had a good starting material. In fact the best liver extracts were made from fresh calf liver and, as I have also shown, fresh livers from other young herbivorous animals were particularly potent. Now, since the livers are disposed according to the directions of the Ministry of Food, these are not available for the preparation of the highly active extracts necessary to save the lives of patients with pernicious anæmia. On the contrary, the manufacturer has to use so-called "pharmaceutical livers"—i.e., livers *unfit* for human consumption that have been rejected in the abbatoirs on account of disease. Even though the more obvious diseased parts may be excised, the very starting product is nevertheless still faulty and contains little—or much less—healthy normal liver tissue, and therefore less of the active principle; in fact in many livers there may be little or no active liver principle even before extraction begins. This means that subpotent liver extracts are produced, and so greater doses are required for treatment, as I have already shown.[1] The same conditions existed during the war in Germany and elsewhere.

These factors have been responsible in great part for the reports of supposed refractoriness to liver extract of many patients with pernicious anæmia, and of long-standing, well-maintained, uncomplicated patients relapsing when put on to these preparations. It is a disgraceful state of affairs, which undoubtedly must have important repercussions in other directions.

Department of Clinical Investigations and Research, University of Manchester. JOHN F. WILKINSON.

SIR,—Dr. McSorley's letter in your issue of Jan. 22 raises the important matter of the dosage of liver extracts required to maintain satisfactory blood-levels in cases of pernicious anæmia, and expresses the opinion that many patients receive inadequate maintenance therapy in this disease.

On the basis of experience at the blood clinic in Edinburgh Royal Infirmary, where several hundred patients with pernicious anæmia report for periodical blood examination, I can subscribe to Dr. McSorley's opinion that 4 ml. of a reliable liver extract is the minimum monthly dosage required for the maintenance of satisfactory blood-levels. I have repeatedly observed that patients tend to relapse when receiving 2 ml. per month—a dose suggested by some manufacturers as indicating the potency of their preparations.

Many cases remain hæmatologically well with a single dose of 4 ml. at intervals of 4 weeks; but some—particularly elderly patients—do better with a 2 ml. injection every 2 weeks. I have found it useful to inquire of the reporting patients whether they feel the need of an injection for a day or so before one is due, and it is surprising how many of them will describe the subjective tonic effect which they come to expect after a liver injection. Any patient who feels this way needs more liver, more often—e.g., 4 ml. every 3 weeks instead of every 4 weeks. The practitioner should remember that a person with pernicious anæmia should and can be made to feel, and remain, in normal health with a consistently normal blood picture, and that the amount of maintenance liver therapy required to achieve this in any given case must be determined by careful observation; but it will rarely be less than 4 ml. per month. It is not usually sufficient to prescribe a monthly dose of 2 ml., as recommended by many manufacturers; for although it may suffice to make the patient feel and look reasonably well, blood examination with this dosage frequently shows subnormal levels; and it is in such cases of inadequate maintenance treatment that the risk of nervous-system complications is very real.

Department of Medicine, University of Edinburgh. JAMES INNES.

SIR,—With reference to your leading article of Jan. 22, everyone concerned with liver extracts will agree on the desirability of having some unitage system for describing anti-pernicious-anæmia potency; and the units should preferably be referable at any time to a standard. It appears probable that some modification of the *Lactobacillus lactis* Dorner assay of vitamin B_{12} will eventually supply the answer.

Since the ultimate touchstone for anti-anæmic potency must be clinical activity, it will be necessary to correlate clinical potency with microbiological activity. Hitherto no attempt has been made to assay quantitatively liver extracts by clinical means, since the number of dose-levels which would have to be employed, and the number of patients on each level, are almost certainly outside the scope of an individual hæmatologist. Clinical assay therefore would have to be done through some official body. In view of the large amount of work entailed, it would be regrettable to initiate such a clinical experiment until all possible steps had been taken to ensure that the results could be generally applied.

Owing to the scanty information published by the original workers on vitamin-B_{12} assay with *Lactobacillus lactis* Dorner (L.L.D.), many investigators in this field have encountered serious difficulties when using this organism. A technique has been evolved in these laboratories which appears to give consistent results and to be free from the earlier difficulties; and an alternative "cup" method for the determination of L.L.D. growth-factors has recently been announced by Cuthbertson.

If a liver extract contained only clinically active vitamin B_{12}, the total L.L.D. activity would measure the clinical potency. Liver extracts are not homogenous, since Cuthbertson and Lester Smith have described a *qualitative* method for demonstrating the *existence* of four different L.L.D. growth-factors in liver extract, some of which have no clinical anti-anæmia activity. In addition Shive has reported the growth effect of ascorbic acid under certain circumstances, and we have produced L.L.D. growth in the absence of liver by autoclaving glucose with certain constituents of the assay medium at certain pH values. It is thus essential to know not only the total Dorner activity of the extract but the number of

1. Wilkinson, J. F. Oliver-Sharpey lectures, Royal College of Physicians, March, 1948. *Lancet* (in the press).
2. Wilkinson, J. F., Israëls, M. C. G. *Ibid*, 1947, ii, 468.

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Dorner factors, the type of each factor, and quantitatively how much each contributes to the total.

The assay method evolved in these laboratories, of which preliminary details are in the press and a complete account is in course of preparation, is sensitive to very small concentrations of L.L.D. growth-factor. It is therefore probable that paper-partition chromatographs could be cut and each strip assayed *quantitatively*, thus giving what would essentially be an L.L.D.-factor "spectrum" for the liver extract tested. This might be expected to show the amount of each factor present in any particular extract. If a number of liver extracts with different spectra were assayed clinically, it would probably be possible to translate vitamin-B_{12} microbiological activity into clinical potency.

Experiments to determine such spectra are at present under investigation in these laboratories. Until the results of these and similar experiments in other laboratories are available, it is perhaps premature to do more than consider a scheme for the quantitative clinical assay of liver extracts.

Evans Biological Institute, Runcorn, Cheshire. GEORGE E. SHAW.

MESENTERIC ADENITIS

SIR,—There has been much speculation on the nature of the colicky abdominal pains in that obscure condition, acute non-specific mesenteric adenitis; and Apley [1] suggests that the pain may arise in the mesentery itself. It seems therefore worth recording the following observation.

On two occasions in the last year while operating on children with this condition (I always operate on these cases, not only because of the dangerous differential diagnosis from appendicitis, but also because I feel that appendicectomy may benefit them) I have followed the small bowel up from the cæcum, being interested to see how far up the glandular enlargement extended, and have found in the mid-small-bowel a small intussusception. In each case it was no more than 1 in. in length; it was easily reducible and would certainly have reduced itself spontaneously.

I feel that such small intussusceptions, which probably form and reduce themselves repeatedly, may explain the colic in this condition.

Leicester Royal Infirmary. PAUL HICKINBOTHAM.

DIABETES

SIR,—As a diabetic for many years, I found the article of Jan. 15 in your disability series extraordinarily interesting, especially as the author's experiences almost coincide with my own. May I offer a few comments?

1. My diabetes was diagnosed as "moderately severe" in 1921, and I therefore had the very trying experience of several years' treatment by diet restriction alone, including fast days and special foodstuffs. Incidentally I was told that with my bad family history I would probably be dead within five years.

2. In 1925, after going slowly but steadily downhill, I was put on 5 units of insulin morning and evening. Although I was still on the same rigid diet the effect of even this small dose was really marvellous. I put on weight steadily, and my very depressed mental outlook reverted to normal within a week or two. Every diabetic, however mild, should receive insulin.

3. With insulin, diabetes is never a real disability, and now with the newer knowledge of dieting brought about by the war and the new types of insulin it is hardly even a "social inconvenience." For at least five years I have been eating the same meals as my wife and family, and my insulin dosage has been steady for about 10 years. I have been very fortunate in having had no serious illnesses and in my work as a medical officer of health.

4. Hypoglycæmic reactions have been and still are my only complications, and I think I have had every type. I have become suddenly unconscious several times, once at a medical meeting whence I was at once removed to hospital and unfortunately diagnosed provisionally as diabetic coma and given insulin pending a blood-sugar estimation, with the result that I did not come to my senses for about 15 hours. Another occasion was in a train, and but for the intervention of a medical friend who happened to be in the same station I would have been removed to the gaol as a "drunk."

I have had as many reactions with globin as with soluble insulin, and unlike the author of your article I have found them just as severe, occurring with very much less warning and developing much more quickly.

MEDICAL OFFICER OF HEALTH.

1. Apley, J. *Post-grad. med. J.* 1948, 24, 588.

AUTORADIOGRAPHY

SIR,—Your annotation last week begins: "Radioactivity was discovered accidentally in 1895." There is a more serious mistake here than a slip in the date. Shortly after the discovery of X rays (which also was not accidental, though lucky) Becquerel set himself to find out whether any of the beautiful fluorescent uranium compounds, which had been prepared or collected over the years by his father and grandfather, "*gave out any rays like X rays*"; the words are his. He found that they did give out rays which had penetrating power and photographic action, and he called the substances radioactive. Röntgen and Becquerel were lucky, one in the sense that Crookes, Lenard, and Schuster were so hot on the track that someone was bound to discover X rays either in 1895 or in 1896. Yet Röntgen did it after being engaged with the problems of the discharge of electricity through gases for a period of only 6 weeks. Becquerel was lucky in having such a père and grandpère; for without them there would have been no laboratory shelves filled with just the test objects he required. They were lucky, but I submit that we have no right to call their discoveries accidental.

London, W.C.1. SIDNEY RUSS.

OSTEOPATHY

SIR,—Several points in the article in your issue of Dec. 25 by Mr. Batchelor and Mr. Cohen call for reply. They refer to the four clinic patients demonstrated to them during their visit as having had their complaints attributed to "displacements" or "subluxations" of spinal vertebræ. This concept of the osteopathic spinal lesion has little place in modern osteopathic teaching, far greater stress being laid on the detection of abnormal tension in the soft tissues around the joints, and fixation or some degree of altered mobility therein. This altered mobility, diagnosed by functional tests applied to the particular area in question, is the final criterion of the presence of a lesion. In certain instances —e.g., in the cervical region—it is possible by radiography in several positions, to demonstrate this lack of articular movement.

Again, the writers refer to "manipulative therapy," and instance constipation as being curable by "lumbar manipulation." It is not the act of manipulation per se which cures, but the release of spinal-joint tension and the restoration of mobility by specific localised techniques. The vital point here is the diagnosis which leads to the application of specific corrective manipulation. The slight alteration of the position of the vertebræ when at rest is merely an aid in the diagnosis, and need not always be completely normalised by the treatment. Mennell is certainly right to stress the necessity of making a diagnosis before manipulation, and the trained osteopath pays great attention to this, particularly to both postural and local unbalance in the body structure.

Those who regard the pathology and local and remote effects of the osteopathic spinal lesion as entirely speculative I would refer to the *Bulletins* of the A. T. Still Research Institute and to the work of Louisa Burns and her associates on this very important subject. I would also refer all those interested in osteopathy to recent literature on the subject and suggest that they do not quote from works which are now of little more than historical interest.

I cannot accept your contributors' view that osteopathic corrective technique is not a "major achievement." Our experience at the British School of Osteopathy over many years' teaching to both medical and non-medical students convinces us that it is by no means simple in the learning. Great patience is needed in teacher and student in the development of a sense of tension—so essential for accuracy in diagnosis and treatment.

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Finally, Sir, may I remind both you and your contributors that it is the non-medical osteopath whose work has gained the confidence of the public, and suggest that it merits consideration as the older of the two schools? I disagree that osteopathic methods have gained much from the work of the so-called "bone-setters," whose manipulations are purely local in purpose and effect. Osteopathic diagnosis and treatment are based on the application of anatomy and physiology and not upon any arbitrary principles.

British School of Osteopathy, London, S.W.1. S. WEBSTER-JONES Principal.

SIR,—Some sweeping statements in your correspondence columns concerning the status of non-medical osteopaths in this country can be modified by facts.

While there may be some 3000 persons claiming to practise osteopathy, only 159 names appear in the current Directory of Members of the Register of Osteopaths, the voluntary body whose institution was recommended by the House of Lords Select Committee. Possibly a further 50 osteopaths practising in the British Isles are eligible, by virtue of their training, for admission to the Register. As for the rest, we fully agree that they may be "doing manipulations completely divorced from what we know of anatomy and physiology." If they display on nameplates the titles quoted by Mr. Pappworth (Jan. 15), there can be little doubt about it; while the contention of Dr. Cyriax (Jan. 22) regarding the patient's welfare and purse is possibly substantiated.

The Register is striving hard to bring these facts to public notice and to enable members of the public to discriminate between the osteopath who has received a proper training, according to the standards advised by the Select Committee, and those who have assumed the title adventurously. Copies of the Directory of Members of the Register are widely distributed.

Members of the Register have voluntarily agreed not to advertise, and we have almost stifled advertising by bogus practitioners by informing many editors and advertising associations of the nature of the ethical code to which our members subscribe.

It is observed that many, for and against osteopathy, have been granted the courtesy of your columns to express their opinions; but that none has, as yet, given evidence that he has sought his opinion from the properly organised section of the profession in its modern form, practising and teaching along the lines suggested by the findings of the House of Lords Select Committee.

General Council and Register of Osteopaths Ltd., 3, Frederick's Place, London, E.C.2. R. F. MILLER Registrar.

SIR,—As president of the London College of Osteopathy, I am anxious to explain exactly what this institution means to the medical profession. The parent body is the British Osteopathic Association, all the members of which hold diplomas from recognised osteopathic colleges in the U.S.A. The diplomas from these six colleges are recognised by statutory enactment throughout the various States in the U.S.A. and in certain provinces in Canada. The present training period in America is at least four years and in some cases five, excluding the pre-osteopathic training in basic sciences, with a further requirement of internship before a diploma is issued.

The British Osteopathic Association, by a majority, resolved upon the creation of the London College of Osteopathy. The members concerned hope that osteopathy may eventually become an integral part of general medical practice. The college aims at giving a sound training in the principles and practice of osteopathy to young medical graduates and possibly to others likely to prove efficient. The college has decided not to take more than 4 or 5 students a year, because personal attention to each student is a very important factor. This outlook is somewhat different from that of the British School of Osteopathy, which boasts of having 30 students.

The course at the London College is a nine-month post-graduate course to medical graduates only, and the instructors are leading osteopaths (medically qualified and otherwise) practising in the London area and near provinces. We are doing everything we can to increase the efficiency of our teaching staff, even to the importing of the finest available exponents from the U.S.A. The American Osteopathic Association recognise that our educational effort at the London College is in a way revolutionary and to some extent experimental, and we do not expect recognition from that body especially for the present. There is also criticism that our course of instruction is not long enough. We, in the London College, do not mind whether the American Association recognise us or not. At the same time it must be thankfully conceded that the American Osteopathic Association are helping us all they possibly can.

The British Osteopathic Association has done all in its power to help the Council and Register of Osteopaths in its effort to become a useful institution to the public. There are, however, many members on the council and register who have not had the training that the association considers necessary. The association does not recognise the British School of Osteopathy. If the school can be made an accredited institution, the association will be pleased; but we doubt whether it is possible for institutions of this type to succeed. They cannot compare with the ordinary medical college in the teaching of basic subjects: their anatomical, physiological, and chemical laboratories are bound to be inferior, and hospital facilities are comparatively negligible.

In the early days of osteopathy, owing to the unfriendliness of the orthodox medical profession, osteopathy was compelled to develop its colleges outside the ordinary medical régime. This habit of education still persists and a large percentage of osteopaths feel that osteopathy would be lost if it became an integral part of general medical education. Nevertheless, the London College will continue to work on the educational basis on which it has started. The only possibility of failure is the lack of patronage by the young medical graduate. The medical profession may oppose us today, but we feel that the medical profession of tomorrow will appreciate what we are doing.

Birmingham. E. T. PHEILS.

*** This correspondence is now closed.—Ed. L.

ADRENALINE AND ITS NEAR RELATIONS

SIR,—Your annotation (Jan. 22) says that isopropylnoradrenaline has a powerful bronchodilator action, but produces tachycardia in animals. Herxheimer,[1] who used this drug in the treatment of asthma, reported that tachycardia was not troublesome, though palpitation was seen in one case.

In investigating the value of this drug in the prophylaxis of postoperative pulmonary atelectasis, results have been promising, but tachycardia has been observed in 60% of a small series; the raised pulse-rate has not led to marked distress, but may adversely affect the postoperative course of a poor-risk patient.

Westminster Hospital, London, S.W.1. C. F. SCURR.

INDEPENDENCE IN RESEARCH

SIR,—Dr. Waddington's courteous letter last week deserves a final reply from me. The "dictum" I cited as having been made by Stalin, I transcribed from a B.B.C. broadcast; and the curious similarity of the words used to those Dr. Waddington had written was illuminating.

Stalin, stung by the public resignations of Professor Dale and Professor Muller from the Moscow Academy of Sciences, made a blustering answer. Following the statement quoted by me, he announced that these eminent professors had been expelled from membership, although they had already publicly resigned several weeks previously; and he described them as "bourgeois reactionaries." Dr. Waddington's version of Stalin's statement bears no date, and it is of course strictly in accordance with Soviet practice to make wholly contradictory versions at different times. The date of their appearance, as indicating current policy, is the only important consideration.

My quotation was made a few weeks ago, and since that date we have been told that the Lysenko doctrine

1. Herxheimer, H. *Lancet*, 1948, 1, 667.

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is to be enforced in Bulgarian science. In a B.B.C. broadcast (Jan. 29) we are informed that Marximoff, a member of the "Politburo" of the Moscow Academy of Sciences, has announced a new decree requiring Soviet physicists to denounce, because they are inconsistent with the doctrines of Marx and Lenin, the new scientific principles based on the quantum theories accepted universally by science outside the Soviet Union; and Professor Bohr, the principal exponent of those theories, is again characterised as a "bourgeois reactionary"—which has become a favourite term of abuse with the Kremlin clique. The University of London at its last award of honorary degrees headed its list with the name of Professor Bohr.

House of Commons. E. GRAHAM-LITTLE.

REGIONAL REPRESENTATION ON THE JOINT TUBERCULOSIS COUNCIL

SIR,—Dr. Sutherland and Dr. England make known through their letter of Jan. 22 that the Joint Tuberculosis Council are at present representing the views of tuberculosis workers on the Central Consultant and Specialists Committee.

The British Tuberculosis Association has, I believe, five or six members on the Joint Tuberculosis Council, one of whom is Dr. England. It is regrettable that no attempt has been made by the association to discover the views of its members on this matter. It would have been more in tune with modern practice if the members of the Joint Tuberculosis Council had sought the views of all tuberculosis workers before they started discussions on the Central Consultant and Specialists Committee.

Carshalton Beeches, Surrey. H. F. HARWOOD.

PREFRONTAL LEUCOTOMY

SIR,—In commenting on our paper of Jan. 15, Dr. Cunningham Dax begins "*Presumably* their results condemn a type of surgical operation. . . . This can however be only *surmise* . . ." In spite of his presumption, far from condemning the operation outright, we in fact say that we wish "to make it quite clear that we do not question the value of prefrontal leucotomy in severe chronic psychotics. We believe that for some . . . leucotomy is at present justified for the results obtained . . . careful judgment must be used in selecting cases from the better type of patient."

We state that our patients were operated upon by Mr. G. C. Knight mostly between seven and three years ago. Those acquainted with the history of leucotomy would know that the standard operation was the procedure used at that time. We did not wish to discuss small variations in sites of incision, as such discussion without anatomical proof is largely speculative. These facts are, however, not so much to the point as is Dr. Cunningham Dax's attempt to add still further to the terminological confusion already existing. He will not help matters by affirming that the name prefrontal leucotomy, *unqualified*, is employed generally to include all the experimental incisions being tried at some places. Our experience is that the term prefrontal leucotomy, unqualified, is used for the standard operation; and we leave it to the reader to judge whether his new or our old and conventional use of the term will lead to the greater confusion.

His further assumption that we used a posterior cut is also wrong; we used the standard operation (*J. ment. Sci.* 1943, **175**, 375) and specifically tried to avoid placing the cut too posteriorly. Dr. Cunningham Dax wants a classification of precise sites of incisions while the patient is alive. We prefer to be guided by the work of Meyer and McLardy rather than by the surgeons' assumed variations or constancy.

Naturally it is desirable to devise a site and extent of section which will produce *therapeutic effect* with a minimal consequent disorder of the personality. But has this been done? If Dr. Cunningham Dax could produce such evidence, including complete and prolonged follow-up, then indeed our paper might become only historically interesting. We ourselves hope, as we stated, that this may come to pass. We would think, however, that part of a sound basis for any such advance would be full and complete knowledge of the effects of the standard operation. Until convincing clinical evidence of the effects of other procedures is forthcoming we must, in the interest of the patients, maintain the position we have taken up, and leave the final opinion to other psychiatrists with experience of the operation.

R. STRÖM-OLSEN
Runwell Hospital, Essex. P. MACDONALD TOW.

SIR,—The history of prefrontal leucotomy is already overloaded with theories and assumptions of the sort Dr. Cunningham Dax advances. Careful systematic studies of available clinical facts and post-mortem material would seem to be more useful than building theories about new cuts without complete evidence of the clinical results or any proof of the exact site and size of the incision. To me, scientific observation in this field is essential from both the basic physiological and from the therapeutic aspects, even though the results may not please Dr. Cunningham Dax.

Severalls Hospital, Colchester. ROBERT H. F. SMITH
Deputy Medical Superintendent.

SIR,—Dr. Cunningham Dax, in his letter of Jan. 22, referred to a broadcast programme upon which, together with a neurosurgeon, Prof. Geoffrey Jefferson, and an anatomist, Prof. J. Z. Young, I gave scientific advice, and cast doubts on the accuracy of the material presented.

The purpose of the programme was to place at the disposal of the listener the present state of our knowledge of the frontal lobes, mainly from the point of view of the relation between mind and body and of the development of social adaptation in man. Most of the illustrative cases were of injury or tumour of the frontal lobes, but the results of leucotomy and its possible effects on social behaviour were inevitably mentioned. Most of the script consisted of quotations or adaptations from scientific papers, and it is difficult to see how Dr. Dax can question their factual accuracy. The author, Mrs. Nesta Pain, enjoys a high reputation in scientific circles for the trouble which she has always taken to ensure accuracy in her scientific programmes. If the effect of the programme has been to make patients and their relatives ask Dr. Dax's team of enthusiasts a few intelligent questions about the long-term implications of the operations which he so frequently advises, I think little harm has been done.

I fully agree with Dr. Dax that the future of this kind of operation lies in limited and accurately localised sections. The correlation of these with their clinical and neuropathological effects offers a field for study which will occupy us for many years to come. The superficial classifications, such as "improved," "relieved," and "not improved," by which the results are at present often assessed, ignore completely any more subtle changes in the patient's attitude to society. The article by Dr. Ström-Olsen and Dr. Tow (Jan. 15) represents, in my opinion, a step in the right direction. The results they have obtained may suggest a note of caution to enthusiasts for this least reversible of the cerebroclastic physical treatments for psychiatric disorder. Scientific follow-up work of this kind, together with neuropathological studies such as are described in Dr. Alfred Meyer's commendable papers, may eventually allow us to develop a sense of proportion with regard to this most valuable new therapeutic approach.

ALEXANDER KENNEDY.
Department of Psychological Medicine, University of Durham.

HOSPITAL ADMINISTRATION

SIR,—If the hospital service is to be really efficient it must take the best from both the former systems. Your contributor last week (p. 193) deals only with one, and like so many who discuss hospital administration makes no reference to the patient, beyond a passing mention in a quotation. The value of the municipal system was that there was a qualified medical man to have the administrative as well as the clinical care of the patient. The lay administrator for a group as described by your contributor can be accepted in broad outline as suitable, provided that in each hospital there is a medical officer in charge with status according to its size.

CHAIRMAN OF MANAGEMENT COMMITTEE.

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NURSING EXPERIENCE FOR MEDICAL STUDENTS

SIR,—Our medical experience is admittedly less than that of Mr. Carruthers and Mr. Richardson. However, we consider that their objection to a limited training in ward routine, expressed in a letter on Jan. 8, is based on false valuation.

One of us is a premedical student, the other a finals science student who hopes to read medicine as soon as he has qualified in science. Like many London medical students we have participated during the past year in a National Union of Students scheme known as "Operation Nightingale," the object of which has been to help Mile End Hospital, and recently Bethnal Green Hospital, at weekends and during vacations.

Most of us, and certainly all medical students, have benefited profoundly from this work. We can now make the bed of a patient suffering from, say, hemiplegia so that he is comfortable; we can appreciate and do our best to abide by a previously rather mysterious and seemingly illogical ward routine; and, most important of all, we feel we have learned something of how best to induce difficult patients to coöperate.

F. CRAMER
M. A. E. SYMONDS.

SIR,—We write as preclinical medical students from the "London" who with others have worked for some time as nursing-orderlies at a general hospital.

Unharassed by near professional examinations, we found the work interesting and instructive during the long academic holidays. The experience gives us preclinical contact with patients and—almost as important—their relatives.

H. J. E. SWAYNE
G. H. BEVAN.

NEW SURGICAL AND GYNÆCOLOGICAL FILMS

SIR,—While it is true that, in theory at least, the integral three-colour systems, which alone are available in 16-mm. film, are not capable of the fine resolution of the monochrome emulsions, in practice the difference is outweighed by other factors; and Mr. Sayle Creer (Jan. 22) is entirely justified in his chiding.

The faults in these cases lie not with the process but with its application. Tolerances in 16 mm. work are small throughout, and errors can quickly accumulate until the final result is unacceptable. Mr. Sayle Creer's list is a good one, but he omits what in my experience is the commonest fault—and the one over which the maker of the film has no control—incompetent projection. The general standard of projection at medical meetings and in the medical schools is incredibly low. This can, of course, ruin the finest film.

ROBERT G. W. OLLERENSHAW.

Department of Medical Photography,
Royal Infirmary, Manchester.

HOSPITAL BIOCHEMISTS

SIR,—In his letter of Jan. 22 Dr. Discombe has expressed opinions on the relative value of science and medical graduates in hospital laboratories which are dangerous inasmuch as, coming from one with his experience, they may be generally accepted.

An industrial concern expecting the highest efficiency from its staff and carrying out analytical procedures comparable with those in a hospital biochemical laboratory, would without hesitation employ a science graduate in preference to a graduate in medicine. What is required in a hospital laboratory is the collection of facts and accurate results from each section; it is then for the director of the department, who should preferably have experience in all branches of clinical pathology, to view the results as a whole and interpret them. The fewer the attempts at interpretation in the preliminary stages the better, as there is a tendency for the results to be coloured by the clinical picture. It is in bacteriology, hæmatology, and histology that the physician and physiologist come into the picture. Let us therefore keep chemistry for the chemists, who alone are competent to deal with the analytical problems.

It is ludicrous to compare the chemistry in the medical curriculum with that of the science degree. In the first instance we have twelve months' training, which is skimped and regarded as something unpleasant to be got rid of and then forgotten as quickly as possible; whilst in the science degree we have whole-time scientific work carried out over a much longer period by those whose chief interest and vocation is science. Is a medical man competent to practise law by reason of his short course in forensic medicine?

Finally, most science graduates are sufficiently competent to hold the post of senior biochemist after three years' experience in an *efficiently conducted laboratory*.

Pathological Laboratory,
Broadgreen Hospital, Liverpool. W. K. TAYLOR.

STREPTOMYCIN IN HUMAN PLAGUE

SIR,—The first table in my letter last week may, as it appeared, be misinterpreted. The meaning of this table was as follows: (1) 9·1% of all the inoculated patients were admitted in a moribund condition, while 18·6% of all the uninoculated patients were moribund; (2) 33% of all the inoculated patients who died were admitted moribund, while out of all the uninoculated patients who died 57% were moribund. The proportion of severe cases was thus lower in the inoculated than in the uninoculated group; and this difference was statistically significant.

S. Y. BHAGWAT.

PENILE CARCINOMA AND CIRCUMCISION

SIR,—In your issue of Jan. 22 (p. 163), Prof. Mahbub Rabbani attributes to me the assertion that "circumcision in Muslims is undertaken at the age of 14 years or later." A reprint has been sent to him of the paper in question, in which, of course, no such ridiculous statement is made.

E. L. KENNAWAY.

Department of Pathology,
St. Bartholomew's Hospital, London, E.C.1.

*** The error, which we regret, is ours alone. Our summary of the British Empire Cancer Campaign's annual report (1948, ii, 192) misrepresented Sir Ernest Kennaway as saying that circumcision is undertaken in Moslems at the age of 14 years or later. Professor Rabbani has kindly corrected this statement.—ED. L.

Public Health

Influenza

In England and Wales there was no important change in the influenza situation up to the beginning of this week. Deaths from this cause in the great towns during the week ended Jan. 22 numbered 45, compared with 40 in the previous week; these are very low figures for this time of year. There have been a few more reports of small outbreaks of a disease which appears clinically to be true epidemic influenza of a mild type; at least one of these could be directly associated with importation from the Continent.

The typing of specimens of virus obtained from the Continent and from cases in this country is not yet completed; but it appears that the virus responsible may be the variant of virus A which appeared in this country on a small scale at the beginning of 1947. If this is so, there is good reason to hope that some measure of immunity has lingered in the population and that a serious epidemic is unlikely.

W.H.O. Epidemiological Broadcasts

In a new world-wide service inaugurated on Jan. 27, the latest W.H.O. information on epidemic diseases and quarantine measures is broadast twice daily from Geneva. This is an extension of the system by which the Pacific and Indian areas have been served by the W.H.O. epidemiological intelligence station at Singapore.

Statistics for London

London County Council has issued a statistical abstract for 1937–1946 [1]; this includes figures for health services.

1. Statistical Abstract for London; 1937–1946, with 1947 figures where available. Pp. 97. 5s. Obtainable from Staples Press Ltd., 14, Great Smith Street, S.W.1.

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Parliament

QUESTION TIME

Funds for Cancer Research

Mr. H. L. AUSTIN asked the Lord President if he would give details of organisations undertaking research work on cancer, detailing their respective financial expenditure per annum.—Mr. HERBERT MORRISON replied: Research on cancer forms an important part of the programme of the Medical Research Council, and approximately £145,000 from public funds are being spent upon it by the council in the current financial year. This sum includes capital expenditure on new forms of radiation apparatus of a costly kind, and on special buildings to house it. Large sums on cancer treatment and research are spent also by the Ministry of Health and by certain hospitals. The principal non-official organisations supporting cancer research in this country are the Imperial Cancer Research Fund and the British Empire Cancer Campaign. Details of expenditure by these bodies are given in their reports. Mr. AUSTIN: In view of the increased incidence of this terrible scourge, and the toll of lives which it takes every day, does the Minister agree that a sum of £145,000, plus the additions he mentions, is really trivial in relation to the problem, and will he not now give serious consideration to increasing the amount of money available for research on this disease?—Mr. MORRISON: If I may say so, one of the functions of Parliament is to protect the taxpayer and the public expenditure. If schemes were put to me whereby probable improvement in our knowledge of cancer could be obtained by the spending of more money I would look at them with favour, but I am not going to spend more money unless I can see that probably good results will be obtained.

Squadron-Leader E. L. FLEMING: Is it not a fact that the total amount contributed by voluntary organisations for cancer research is much greater than the £145,000 contributed by the Government?—Mr. MORRISON: I do not know, but it may well be so and that should be taken into account.

Mr. J. LEWIS: Is the Minister aware that the answer he has given in regard to cancer research is precisely the same as that which he gave to me when I raised the question of the common cold? Will he continue to bear in mind that one cannot tell the result of scientific research until the money has been spent?—Mr. MORRISON: It is quite likely that the answer is the same and will continue to be so for similar questions.

Treatment Abroad

Mr. G. W. ODEY asked the Chancellor of the Exchequer the names of the Exchange Control Advisory Committee who dealt with applications for foreign exchange for the purpose of medical treatment abroad; how frequently they met; and what was the date of their last meeting.—Sir STAFFORD CRIPPS replied: The members of the committee are all distinguished medical specialists, but I do not think that it would be advisable to disclose their names. The committee meets every two or three months for consideration of matters of policy and points of principle. The last full meeting was held on Oct. 20, 1948. Individual applications are considered by two or more members of the committee. If they are in agreement their decision is accepted. In the event of disagreement, or in cases of doubt, further members of the committee are consulted and if necessary the opinions of outside specialists are obtained.

Industrial Diseases

Mr. RONALD WILLIAMS asked the Minister of National Insurance whether he could now say what steps he proposed to take regarding the report of the Departmental Committee on Industrial Diseases.—Mr. JAMES GRIFFITHS replied: I have now considered the report of this committee further in the light of the advice I have received from the Industrial Injuries Advisory Council. I do not think any immediate alterations in the regulations are called for, but in my administration of part IV of the Act, which deals with the extension of insurance to diseases, I shall be guided by the principles laid down in the report. As regards the committee's proposal that a special committee should be set up to deal with the various matters set out in paragraph 37 of the report, the council point out that in view of their statutory functions they are the appropriate body to advise me on these matters. I accept this view and am accordingly arranging that any necessary examination of such questions should be undertaken by a subcommittee of the council which would have power to call for such expert assistance as they might require.

Purchase-tax on Drugs

Replying to a question Sir STAFFORD CRIPPS stated that about £5½ million of purchase-tax had been paid, at the rate of 33⅓%, in respect of drugs and medicines delivered by registered manufacturers and wholesalers during the period Nov. 13, 1947, to March 31, 1948; the receipts at the rate of 16⅔% for the period April 1, 1947, to Nov. 12, 1947, were approximately £5 million.

Scottish Teaching Hospitals

Miss MARGARET HERBISON asked the Secretary of State for Scotland which hospitals had been added to the list of teaching hospitals since June, 1946.—Mr. ARTHUR WOODBURN replied: The bulk of medical teaching in Scotland is carried on in a few large general hospitals in the four centres, Aberdeen, Dundee, Edinburgh, and Glasgow, and the main teaching hospitals remain as in June, 1946. There is, however, an increasing use of other hospitals for teaching purposes both in the four centres and outside, and, in the interests of the hospital service as well as teaching, I am anxious to encourage this extension. Medical-education committees to advise the regional hospital boards on this and other aspects of the provision of facilities for clinical teaching are about to begin work in each region.

Cost of the National Health Service

Sir THOMAS MOORE asked the Minister of Health what was the latest estimate for the current annual cost of the National Health Service, as divided amongst the main branches, together with the administration costs; and if he would also give figures indicating the estimated income from contributors.—Mr. A. BEVAN replied: A supplementary estimate of the cost of the National Health Service for the period July 5, 1948, to March 31, 1949, divided among the main branches, will shortly be laid before the House. The amount available from National Insurance contributions towards the cost of this service is estimated to be £24 million for the period in question.

Doctors' Final Payments

Mr. FRANK BESWICK asked the Minister when he expected to make a final payment under the former National Insurance scheme to medical practitioners in Middlesex.—Mr. BEVAN replied: Executive councils have now been notified of the amounts available for the final payments to doctors in respect of medical benefit under the National Health Insurance Acts and have been asked to make the necessary payments to doctors as soon as possible.

Medical Officers' Salaries

Mr. WILLIAM KEENAN asked the Minister what steps he proposed to take to help or assist local authorities to secure and retain the services of medical officers now that the salaries paid and offered were considered insufficient since the operation of the Health Service Act of July last.—Mr. BEVAN replied: While expressing no view on the adequacy of these salaries, I am ready to join with the local authorities in establishing a medical Whitley council on which they can be discussed.

Independent Dental Mechanics

Mr. E. A. BRAMALL asked the Minister if he was satisfied that dentists could cope with the volume of work involved in providing dentures under the National Health Service without the assistance of dental mechanics working independently of dentists; or what steps he was taking to amend the Act.—Mr. BEVAN replied: While there are not at present enough dentists to treat without delay all those desiring to take advantage of the National Health Service, I should not think it right, in view of the findings of the Teviot Committee, to seek to extend the statutory limits to the functions of dental technicians. The proper remedy is in my view to increase the number of dentists.

Epileptic Colonies

Mr. CHARLES ROYLE asked the Minister if he would bring colonies for sane epileptics under the provisions of the National Health Act, 1946.—Mr. BEVAN replied: The National Health Service provides treatment, but not residential care such as these colonies give. This is the responsibility of the local welfare authorities under the National Assistance Act.

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Obituary

FREDERIC JEUNE WILLANS

K.C.V.O., M.R.C.S.

Sir Frederic Willans, surgeon-apothecary to His Majesty's household at Sandringham since 1924, died on Jan. 26 at the age of 65. The son of the late Dr. W. Blundell Willans, he was born at Much Hadham, in Hertfordshire, and educated at Framlingham College. He studied medicine at the University of Durham and at the London Hospital, from which he took the Conjoint qualification in 1910. Shortly afterwards he settled in practice at Sandringham where, but for his service with the R.A.M.C. during the 1914-18 war, he remained for the rest of his life. Sir Frederic was formerly surgeon-apothecary to Queen Alexandra. In 1923 he was appointed M.V.O.; he was promoted C.V.O. in 1925 and K.C.V.O. eight years later. In 1916 he married Wynefred, only daughter of the late Sir Alan Manby, of Sandringham.

PHILIP HEWER WELLS

M.C., M.R.C.P.

Dr. Philip Wells, who died on Jan. 17 at Stratford-on-Avon at the age of 56, was the third son of the late Mr. A. P. L. Wells, senior surgeon to the Central London Ophthalmic Hospital. On his mother's side he also came of a medical family and he had intimate connexions with St. Bartholomew's Hospital, from which he qualified in 1915. During his distinguished career as a student he was awarded the Brackenbury scholarship, the Kirkes scholarship and medal, and the Willett medal, and was elected president of the Abernethian Society. After acting as house-physician to Lord Horder he joined the R.A.M.C. and was appointed medical officer to the 2nd battalion of the Coldstream Guards, a regiment of which he remained immensely proud. Within eighteen months he was awarded a Military Cross and bar, and later he served a short period in Russia. Returning to civil life he acted as house-physician at the Radcliffe Infirmary, Oxford, taking the M.R.C.P. in 1923. Later he joined his uncle, Earnshaw Hewer, F.R.C.S., in general practice in Stratford-on-Avon.

At the beginning of the late war, as medical specialist to the 10th British General Hospital, Wells was posted to France. After the evacuation he held a number of positions until, in 1943, whilst acting as consulting physician to the South-Eastern Command, his health broke down and he was invalided out of the Service with the rank of lieut.-colonel. On his return to Stratford, with great courage he continued his work as long as possible.

A man of great physical strength and a fine athlete, he was an excellent player of ball games, in which he delighted. But with all his qualifications he will be best remembered for his forceful personality, his spontaneous generosity, and his uncompromising defence of what he considered to be right. He leaves a widow, two sons, and two daughters.

HUGH AUGUSTINE RICHARDS

M.A., M.R.C.S., F.F.A. R.C.S.

Dr. Hugh Richards, consulting anæsthetist to King's College Hospital, died on Jan. 22, at the age of 64, while on holiday at Grenada, British West Indies.

Educated at Rossall and at Clare College, Cambridge, he qualified from King's College Hospital in 1913. After a brief interlude in resident appointments and as a ship's surgeon with the Orient line, he served from 1914 to 1916 as a surgeon in troopships, and thereafter with a casualty-clearing station in France. A year after his demobilisation in 1920, he was appointed assistant anæsthetist to King's College Hospital; and in 1935 he became senior anæsthetist—a post which he held until his retirement in 1946. He was given the D.A. in 1936, and last year was awarded the fellowship of the new Faculty of Anæsthetists. He served the anæsthetics section of the Royal Society of Medicine as secretary and later as president. In September, 1939, he gave up a flourishing practice to take a full-time post in the Emergency Medical Service; and throughout the war he worked at Horton Emergency Hospital, where he organised the anæsthetic services as well as taking his share of the routine work and continuing to teach students and train residents.

Hugh Richards had nothing of the trimmer in his character; in all things he saw only the right and the wrong way, and throughout his life he adhered unhesitatingly to the principles he had laid down for himself. Some were put off by his brusque and uncompromising manner, but those who troubled to look beneath this façade found sincerity and loyalty. Trained at King's he was essentially a King's man, giving the hospital his ungrudging support.

It was the same in the field of anæsthetics. For many years ether had been his friend and servant, and so he was not easily led away by new methods. As a giver of ether he was unsurpassed, and there was some justification for his claim that his results with this agent were equal to those obtained in any other way; certainly the surgeons for whom he worked agreed with him. Like many who set themselves high standards he contributed little to the literature on his subject. It was as a teacher that he gave his greatest service. His instruction was firm and dogmatic, and he taught with zest, keeping always to fundamental principles. Many an unfortunate student quailed under his blast of sarcasm, but this was merely part of a well-tried method; his students did not make the same mistake twice. Despite his somewhat gruff manner with them he was genuinely interested in student activities; when he first joined the staff he played a considerable part in reviving the hospital hockey club, and he retained his interest in this, and in the rugby club, until he retired. For many years he was treasurer, and during his last five years president, of the students clubs and societies union—an organisation which flourished under his shrewd management. By his unexpected death King's has lost a real personality and a staunch supporter, and many members of the staff a true friend.

Shortly before his retirement Dr. Richards married, and his widow survives him.

V. F. H.

Births, Marriages, and Deaths

BIRTHS

ARNOTT.—On Jan. 23, in London, to Dr. Ruth Arnott (née Burt), the wife of Dr. D. C. Arnott—twin sons.

BROOKS.—On Jan. 22, at Swanage, the wife of Dr. T. H. P. Brooks—a son.

FORBES.—On Jan. 22, at Oxford, the wife of Dr. H. A. W. Forbes—a daughter.

HALL.—On Jan. 25, at Dover, the wife of Dr. Derek Hall—a daughter.

HOLLIS.—On Jan. 17, the wife of Captain D. G. H. Hollis, R.A.M.C.—a son.

LE VAY.—On Jan. 28, in London, to Dr. Marjorie Le Vay, the wife of Mr. David Le Vay, F.R.C.S.—a son.

MCQUEEN.—On Jan. 22, in Birmingham, the wife of Dr. E. G. McQueen—a daughter.

MAURICE.—On Jan. 25, at Marlborough, the wife of Dr. T. R. Maurice—a daughter.

WRIGHT.—On Jan. 27, at Gloucester, the wife of Dr. Benjaman Wright—a daughter.

WRIGHT.—On Jan. 15, at York, the wife of Dr. W. R. Wright—a daughter.

MARRIAGES

FISHER—CLIVE.—On Jan. 22, in London, Alfred George Timbrell Fisher, M.C., F.R.C.S., to Edith Frances Clive.

MCCAMMON—CHAMNEY.—On Jan. 22, at Swindon, Wilts, Francis Alexander McCammon, O.B.E., M.C., colonel, A.M.S. retd, to Eileen Chamney.

DEATHS

CONNAL.—On Jan. 26, at Aberdeen, Andrew Connal, O.B.E., M.D. Glasg., D.P.H., D.T.M. & H.

DODDS.—On Jan. 27, Robert Leslie Dodds, M.CH. Belf., F.R.C.S., F.R.C.O.G.

FENN.—On Jan. 23, at Bath, the Rev. Albert Gershom Fenn, M.B. Edin.

JONES.—Presumed lost at sea, Crawford Maxwell Jones, M.B. Edin.

KELLY.—On Jan. 29, in London, Thomas Bernard Kelly, D.S.O., F.R.C.S.E., colonel, I.M.S. retd.

MARTIN.—On Jan. 26, Charles de Carteret Martin, M.D. Edin., D.T.M. & H.

RICHARDS.—On Jan. 22, in Grenada, British West Indies, Hugh Augustine Richards, M.A. Camb., M.R.C.S., D.A.

SPURRELL.—On Jan. 26, at Frowen, Carmarthen, Charles Spurrell, F.R.C.S., aged 82.

WILLANS.—On Jan. 27, at King's Lynn, Frederic Jeune Willans, K.C.V.O., M.R.C.S.

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Notes and News

THE OVERFED CHILD

THAT nine-tenths of the diseases of infancy and childhood are due to overfeeding was the thesis maintained before the Devon and Exeter Medico-Chirurgical Society last month by Dr. J. H. Gibbens. He had observed that of 1500 children seen at welfare centres and hospital outpatient departments and in private practice, more than half had had their tonsils removed by the age of 5. Tracing back the medical histories of such children he had found a recurrent syndrome in which the first departure from normal, noticed in infancy, was a sharp and sudden gain in weight. This obesity, due not to fat but to fluid retention, was associated with poor muscle-tone leading to orthopædic disorders. Secondly, there were disturbances affecting the liver and gastro-intestinal tract. Thirdly, there was a group of mental symptoms comprising irritability and fretfulness, refusal or pouching of food, food-fads, insomnia, and enuresis. Metabolic disturbances affecting the skin, such as infantile eczema, or affecting the mucous membranes, such as asthma, were also noted. Finally a breakdown in immunity resulted in recurrent attacks of tonsillitis, otitis media, and bronchitis, and ended in tonsillectomy, which often failed to cure the catarrhal state.

In the early stages, Dr. Gibbens said, these children presented a fairly constant picture: they were fat, flabby, and pale but not anæmic. Sometimes they had livid extremities suggesting a "chilblain" circulation. There was watery obesity, especially of the thighs. Muscle-tone was poor and they did not crawl properly. This condition, described by Czerny as the "exudative diathesis" and by Finkelstein as the "lymphatic diathesis," resembled the allergic state and was characterised by large watery tonsils and sometimes by a spleen palpable without apparent cause. The thymus was enlarged and the condition might end in status lymphaticus and thymic death. Difficult dentition occurred exclusively among these fat, flabby children, and in boys more than in girls because mothers tended to "stuff" boys under the impression—laudable but mistaken—that by doing so they would make them strong. Other possible sequelæ of overfeeding were pylorospasm, leading to pyloric stenosis (wrongly called congenital), convulsions, intussusception, rickets, chilblains, impetigo, and recurrent boils and styes. Dr. Gibbens contended that if these cases were caught early at the stage of sudden rise in weight, the melancholy chain of events described would not develop, provided that their food intake was sensibly restricted: in the case of breast-fed infants the restriction must be applied also to the mothers.

ECTOPIA VESICÆ AND CHILDBEARING

AT a meeting of the North of England Obstetrical and Gynæcological Society on Jan. 21, Dr. Walter Calvert described the case of a patient who in childhood had had the ureters transplanted into the colon, and the bladder excised, for ectopia vesicæ. Thereafter she led an active, ordinary life. After marriage she had a successful vaginal plastic operation for dyspareunia and later she conceived. During pregnancy there was renal insufficiency, and near term cæsarean section with sterilisation was performed, a healthy child of 6 lb. 12 oz. being delivered. Recovery was uneventful.

DOCTORS ENTERING AUSTRALIA

IMMIGRANT doctors cannot register for medical practice in Australia unless they hold degrees from medical schools in the United Kingdom, Australia, New Zealand, Northern Ireland, or Eire, or from certain further specified schools within the British Commonwealth. Doctors holding degrees obtained, after at least five years' study, at any other medical school may register after passing the 4th-year, 5th-year, and final examinations at a recognised Australian medical school; thus it is at least three years before an immigrant doctor can obtain a licence to practise. The only exception is in Western Australia, where local rules allow an immigrant doctor to obtain regional registration if he or she is willing to practise where the State government directs; the object of this regional registration, which is seldom granted and is reviewed each year for seven years, is to obtain doctors willing to remain in remote centres. Doctors intending to migrate should consult the medical registration board of the State in which they wish to settle.

Refugee doctors have been going to Australia since the early '30s. Since November, 1947, about 10,000 displaced persons have arrived under contract to work for two years under direction; among these 10,000 there have been about 20 qualified medical men, who have been employed mostly as medical orderlies to work out their two years' contract. If they are conveniently situated there is no official objection to their studying part-time and taking some of their Australian qualifying examinations during their contract period.

HOSPITAL CATERING TRAINING-CENTRE

UNDER the auspices of King Edward's Hospital Fund for London, a centre is to be established at St. Pancras Hospital (now part of University College Hospital), where training will be offered in all branches of hospital catering. The intention is to make this centre, which will provide meals for patients and staff in the hospital, a model in layout, organisation, and equipment; it will include all modern labour-saving devices. It will, however, be at least 6–12 months before the centre is ready to take trainees. The officer-in-charge will be Mr. C. C. A. Gibbs, who for the past three years has been catering officer to St. Mary's Hospital, London.

University of Oxford

On Jan. 20 the following degrees were conferred:

D.M.—Frank Hampson.

B.M.—Thomas Bell, D. G. Jamison, J. T. H. Green,* T. H. C. Lewis,* A. H. Campbell.*

* In absentia.

University of Cambridge

On Jan. 21 the following degrees were conferred:

M.A.—Joan M. Boissard, J. W. Millen.

M.B., B.Chir.—R. D. Allen,* J. A. Balint,* June Bean,* G. P. Blanshard,* T. B. Boulton,* Alexis Brook,* R. C. Cundall,* P. G. R. Dench,* J. V. Earle,* J. R. Edsall,* H. E. Flint,* D. R. Harrocks,* E. W. Heining, G. R. Hervey, A. R. H. Hicks,* J. B. Howells, G. M. Jones,* G. A. D. Lavy,* K. W. Leech,* D. E. Lewin,* Leslie Linder, J. D. *Llywelyn-Jones,* P. H. Lord,* C. B. McKerrow,* J. L. Millard,* G. C. Myddleton,* T. M. Robinson,* R. A. Rowan,* F. R. Ryle,* K. H. L. Scougall,* R. S. Smith,* C. D. Thompson,* T. H. H. Wade, T. J. D. Walker,* J. C. Wardill,* A. L. Wells,* N. P. L. Wildy,* R. B. Wright,* J. G. O. W. Yerburgh.*

* By proxy.

University of London

The degree of D.SC. has been conferred on Dr. Hans Grüneberg.

University of Bristol

J. B. Brierley's dissertation for the M.D. degree has been approved.

University of Manchester

Dr. R. S. F. Schilling has been appointed reader and Dr. Stanley Wyatt lecturer in occupational health.

Royal College of Physicians of London

At a meeting of the comitia of the college held on Jan. 27 with Lord Moran, the president, in the chair, the following, having satisfied the censors' board, were elected to the membership:

D. M. Abelson, M.B. Lond., L. E. Arundell, M.B. Birm., John Badenoch, B.M. Oxfd, R. G. Benians, M.B. Camb., E. R. Bickerstaff, M.D. Birm., J. D. Blainey, M.B. Lond., J. P. P. Bradshaw, M.B. Lond., B. C. Brown, M.D. Western Ontario, P. E. Brown, M.B. Lond., flight-lieutenant R.A.F.M.S., Alice M. Bush, M.B. N.Z., R. J. Calvert, M.B. Glasg., K. M. Chalmers, M.B. Edin., J. B. Cochran, M.B. Glasg., J. S. Crowther, M.B. Lond., Dewi Davies, M.B. Lond., J. F. Delafresnaye, M.D. Paris, M.B. Lond., E. M. C. Dunlop, M.D. Lond., T. B. Dunn, M.B. Edin., G. F. Edwards, M.B.E., M.B. Lond., major R.A.M.C., H. L. English, M.B. Camb., O. D. Fisher, M.B. Lond., R. M. Forrester, M.B. Camb., J. M. Garvie, B.M. Oxfd, P. B. B. Gatenby, M.B. Dublin, H. J. Goldsmith, M.B. Lond., Alan Grant, M.D. Aberd., A. P. Grant, M.D. Belf., L. J. Grant, M.B. Lond., Isaac Grayce, M.B. Cape Town, C. W. E. B. Greaves, L.R.C.P., D. McR. Hanna, M.B. N.Z., T. D. B. Hanratty, M.D. N.U.I., P. L. de V. Hart, M.B. Lond., F. G. J. Hayhoe, M.B. Camb., C. B. Henderson, M.B. Durham, A. C. S. Hobson, M.C., L.R.C.P. major R.A.M.C., G. K. H. Hodgkin, B.M. Oxfd, K. S. Holt, M.B. Manc., J. N. Horne, M.D. Camb., W. M. Irwin, M.B. Adelaide, E. W. Jackson, M.D. Leeds, D. V. M. Jones, L.R.C.P. N. B. Jones, M.B. Lpool, P. G. Keates, M.D. Lond., Madeline K. Keech, M.B. Lond., M. A. Khan, M.B. Punjab, L. G. Kiloh, M.B. Lond., Richard King-Brown, M.D. Lond., W. M. Lancaster, M.B. Glasg., David Lawrence, M.D. Lond., J. C. Macaulay, M.B. Lond., R. B. McConnell, M.B. Lpool, E. L. McDonald, M.B. Camb., A. E. Macintosh, M.B. Aberd., Angus McPherson, M.B. Lpool, R. I. Meanock, M.D. Lond., A. P. Meiklejohn, B.M. Oxfd, D. E. Meredith, M.D. Lond., Clarence Merskey M.D. Cape Town, M. J. Meynell, M.D. Sheff., E. F. D. Montuschi, M.D. Florence, David Morris, L.R.C.P. B. K. Naik, M.B. Bombay, L. D. Osler, M.B. Camb., R. T. Parkin, M.B. Lond., Jack Pepys, M.B. Witwatersrand, G. W. Poole, M.B. Birm., S. R. Reader, M.B. Sydney E. A. Ritchie, M.B. Lond., A. J. Robertson, M.B. Lpool, L. J. Rowley, M.B. Camb., Eric Sanders, M.B. Lond., L. G. Scott, M.B. Lond.,

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K. R. Shroff, M.B. Bombay, J. A. Simpson, M.B. Glasg., Stanley Smith, M.D. Leeds, A. E. Thomas, M.B. Manc., A. D. Thomson, M.B. Camb., D. Q. Trounce, M.B. Lond., J. S. Watson, M.B. Lond., R. W. E. Watts, M.B. Lond., captain R.A.M.C., I. G. Wickes, M.B. Camb., J. R. Wilson, M.B. Lond., R. A. Womersley, M.B. Camb.

Licences to practise were conferred upon the following 134 candidates (108 men and 26 women) who have passed the final examination of the conjoint board and have complied with the by-laws of the college:

L. A. A. Adams, Mari Ainsleigh-Jones, R. D. Allen, Anthony Allibone, D. W. Anniss, Mary P. Armstrong, Patricia Arnold, A. H. W. Bain, J. A. Balint, A. A. Bartholomew, D. A. A. Beardsmore, Thomas Bell, L. C. Bellsham-Revell, J. F. Bennett, C. A. Biscoe, I. F. Bishop, J. B. F. Boyle, Maria E. B. Brennan, Sylvia M. Brown, T. W. Brown, T. V. Campkin, Jack Cantor, J. W. Cieszynski, K. M. Citron, W. E. Clifford, O. F. Conran, G. A. Coombs, F. H. Corbitt, E. H. J. Cotter, Patricia Q. Currie, T. A. Daff, Shirin Dastur, G. L. Davies, Joyce M. Daws, J. M. Dodd, G. H. Dunkerley, Audrey M. Emmerson, J. B. C. Evelegh, J. G. Fairer, Otto Fleischner, H. E. Flint, Margaret Ford, A. T. T. Forrester, P. G. Fox, Elizabeth M. France, Jean M. Gibson, J. G. Gill, U. S. Gill, R. G. Godfrey, M. M. Gollow, A. J. Graham, J. C. Graham-Stewart, Murray Grant, Margaret I. Green, D. G. G. Greenaway, Wendy E. Greengross, D. H. Griffiths, A. K. Hancock, D. T. G. Harris, Kathleen J. Harrison, Gladys F. Horton, E. T. Hughes, T. J. M. Hughes, D. S. Hurwood, J. M. E. Hyde, Bernard Jacobs, A. V. Jenkins, D. G. Jenkins, I. M. Jones, Gerald Keen, P. W. L. Kelly, Michael Lauchlan, Joan E. Lewis, Thomas McKendrick, D. J. Mantle, Ida Mather, A. H. Mendoza, G. G. Meynell, J. L. Millard, Roger Mitchell, G. W. Moore, J. H. S. Morgan, Dennis Morris, B. C. Morson, G. V. Mulholland, J. G. B. Myles, Chamanlal Nagrath, E. J. Newton, J. G. Noble, Kenneth Orr-Hughes, D. N. H. Owen, N. C. W. Owen, Joyce M. Parker, J. E. Phillips, Stephen Plumpton, Benno Pollak, K. G. Prior, D. S. Richardson, I. H. Richardson, R. E. Richardson, Kathleen M. Roby, Peter Ronchetti, P. T. C. Rowan, J. E. Russell, G. W. Scott, T. B. Scott, A. M. Sellars, F. M. M. Shattock, Muriel E. Sidaway, Albert Southwell, H. W. Stanley, Ursula Stanley, A. E. Steel, R. R. Stephens, Sara I. Stinson, Elizabeth J. Sutton, Brenda A. Taylor, C. W. Taylor, G. B. Taylor, Mavis B. Taylor, J. N. R. Toke, D. O. Topp, G. J. Van Klaveren, I. S. Waller, R. D. Walsh, A. J. Walters, Monica Watson, P. S. Watson, J. D. Wheatcroft, I. C. L. White, D. A. G. Williams, J. D. Williams, T. E. Williams, G. T. Woods.

Diplomas were granted to those named in reports of meetings of the Royal College of Surgeons (*Lancet*, 1948, ii, 996; Jan. 22, p. 169). The following diplomas were also conferred:

D.P.M.—J. C. Baillie, R. F. B. Bennett, F. H. Bodman, E. A. Burkitt, F. R. M. Calder, Sydney Catterall, G. I. Davies, R. H. Gaman, J. K. Hewat, R. M. Jones, F. J. Kelleher, Harold Lantin, Ivan Leveson, Amedeo Limentani, S. C. MacMillan, J. W. Macpherson, D. H. D. Paine, B. W. Richards, R. A. Sandison, R. B. Taylor, W. N. Taylor, D. C. Watt, Alexander Wood, C. M. Xavier, F. L. D. Young.

D.L.O.—H. J. Doran, T. C. Fort, R. M. Harvey, D. J. Heffernan, J. B. O'Mahony, A. R. Rowe, Rustomjee Cawasjee Jamshedjee Rustomjee, J. L. Wakelin.

D.M.R.-D.—C. J. Alexander, C. W. P. Bradfield, R. G. Britt, J. H. L. Conway-Hughes, A. M. Fraser, P. H. K. Gray, C. H. Kitchen, R. E. Lawrence, Ronald Levy, R. H. C. Manifold, Stephen Moor, N. D. W. Morrison, Richard Paul, J. McK. Reid, H. L. Ross, Martin Spiro, J. L. Steven, B. A. Stoll, D. R. Syred, E. J. S. Townsend, R. F. Williams.

D.P.H.—Ralph Alexander, H. J. Anderson, Roshan Lall Chopra, Daniel Coueslant, C. D. Edwards, B. M. George, D. E. Jeremiah, B. G. Johnsen, Atam Parkash Kalra, A. P. R. Lewis, D. K. L. Lindsay, W. D. H. McFarland, C. W. Maisey, Dorothy K. Paterson, F. O. Potter, Annie E. G. Rowlands, Joan N. Ruben, Victoria M. D. N. Shaw, Margaret S. Stevenson, R. N. E. Watt, Peter West, J. L. M. Whitbread.

D.M.R-T.—I. G. Brown, H. G. Frank, W. D. Fraser, Robert Gibb, Prabhat Kumar Haldar, Eileen H. Harrison, G. M. Holme, A. E. Jones, A. H. McCallum, J. R. MacLeod, R. D. Nash, Uma Shankar Prasad, T. M. Prossor, W. M. Ross, Nirode Bijali Roy, P. B. Woodyatt.

Royal College of Surgeons of England

On Monday, Feb. 14, at 5 P.M., Mr. H. S. Souttar will deliver the Hunterian oration at the college. He has chosen as the title of his discourse John Hunter—the Observer.

Congress of Electro-encephalography

The second International Congress of Electro-encephalography will take place in Paris on Sept. 1, 2, and 3 under the presidency of Dr. A. Baudouin. Further information may be had from Mr. W. Grey Walter, D.SC., Burden Neurological Institute, Stoke Lane, Stapleton, Bristol, or from Dr. H. Gastaut, 149, Promenade de la Corniche, Marseilles.

Conference on Mental Health

Sir Wilson Jameson will give the introductory address at a conference which the National Association for Mental Health is holding at Seymour Hall, Seymour Place, London, W.1, on March 17 and 18. Other medical speakers will include Prof. D. R. MacCalman and Prof. J. C. Spence. Further information may be had from the conference secretary, 39, Queen Anne Street, W.1.

Institute of Sociology

A meeting of the institute will be held on Tuesday, Feb. 22, at 5.30 P.M., at the Royal Institute of British Architects, Portland Place, London, W.1, when Dr. G. Scott Williamson will speak on the Family as a Basis of Society.

Congress of Social Climatology

An international congress of social climatology will be held at Villard-de-Lans, Isère, France, on March 25, 26, and 27 under the presidency of Professor Debré. Further information may be had from the secretary, Dr. Terrel, Villard-de-Lans.

International Congress of Comparative Pathology

The dates of this congress, which is being held at Istanbul, have been changed to April 22 to 29. Further information may be had from Prof. N. R. Belger, Taksim, Siraserviler 75/3, Istanbul, Turkey, or Mr. R. E. Glover, the hon. secretary of the British national committee, Royal Veterinary College, London, N.W.1.

Nuffield Fellowships in Dentistry

The Nuffield Foundation are offering fellowships and scholarships to men and women with medical, scientific, or dental qualifications who wish to receive further training to fit them to undertake teaching or research in dentistry. Further information will be found in our advertisement columns.

Society of Registered Male Nurses

Speaking at the dinner of this society on Jan. 26, Mr. John Edwards, parliamentary secretary to the Ministry of Health, declared that, though hospitals were still short of their full complement of nurses and midwives, the situation was steadily improving. The number of male nurses at September, 1948, was 23,000—double the number four years ago. Of 486 male candidates who took the intensive courses for ex-Service men and women who had had experience as nursing orderlies, 446 had been successful in the final State examination. Mr. Edwards thought it unfortunate that men were usually recruited to nursing later than women. He hoped this could be altered, and then male nurses in the mental field could take both general and mental training, thus bettering their chances of promotion. He specially urged mental nurses who had an aptitude for it to take up teaching, and said the Ministry were considering how increased financial help could be given to candidates for tutors' courses. Dr. Leslie Banks, representing Sir Wilson Jameson and the medical staff of the Ministry, traced the history of male nurses from the time of the monasteries, and said he felt there was a field for male nurses in district work, in short-stay hostels, and in clubs for the aged and infirm and psychiatric social clubs, as well as hospitals. Prof. Frances Zeigler, dean of the Vanderbilt School of Medicine, U.S.A., said that coeducation in nursing was recommended in America.

Parliamentary and Scientific Committee

At a luncheon held by this committee in London on Jan. 27 Sir John Anderson, F.R.S., M.P., the president, said that the Spens report on payment of medical specialists had had very wide repercussions, and unless action was taken there might be a disastrous drift away from academic and Government posts. He referred with regret to the approaching retirement from the Civil Service of three of its most eminent scientists, Sir Edward Appleton, F.R.S., Sir Charles Darwin, F.R.S., and Sir Edward Mellanby, F.R.S. Sir Charles Darwin said that the scientific Civil Service was now a very important organ of Government; yet it was attracting lamentably few recruits, and now had hardly anyone between the ages of 30 and 45. Its members had been kept at full stretch for ten years, and the habit of keeping all reserves in the front rank threatened to bring calamity. It should be recognised that not all research-workers were men of the inspired type like Faraday: research was a profession like other professions which people entered because it offered good pay and prospects. Conditions had to be created in which second-rate men could do first-rate work: and here and there among the recruits would be those with the divine spark who would change the world. The task of politics was to accommodate people to their greatly changed surroundings, and one of the difficulties was that man did not want to work at all but was only happy when working rather hard.

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Blackwell Centenary

Dr. Helen Mackay was among the women doctors who received centennial citations at the convocation held at Geneva, New York State, by the Hobart and William Smith Colleges to celebrate the centenary of the graduation of Elizabeth Blackwell, the first woman on the British Medical Register.

Chemists Federation

At this federation's annual luncheon in London last week, Dr. C. H. Hampshire suggested that the voluntary control of pharmaceutical specialities was only a beginning; almost inevitably the Government would eventually interest itself in this matter. Dr. Charles Hill reasoned that the responsibility should remain with the profession and trade.

Royal Medical Foundation of Epsom College

The foundation has available the following:

One or two *St. Anne's Scholarships* for girls attending Church of England schools. Candidates must be fully 9 years of age and the orphan daughters of medical men who have been in independent practice in England or Wales for not less than 5 years.

Pensions for necessitous medical men fully 55 years of age, provided they have been registered for 5 years, and for the widows of medical practitioners who are 60 years and upwards.

Scholarships and grants for children of either sex, not necessarily orphans. Candidates must be of public-school age.

Grants from the Eastes Trust for the relief of registered members of the profession of any age, or their widows or orphans, and for the educational assistance of their daughters or sons.

Forms of application may be had from the secretary, Epsom College, Surrey.

Hospital Congress

The first International Hospital Congress is to be held in Holland at Amsterdam and Groningen from May 30 to June 4, when the constitution of the International Hospital Federation, provisionally agreed at Lucerne in 1947, will be approved. Prof. René Sand will preside over the congress and the discussions will include the Influence of Economic and Social Changes on Hospital Administration; the Training of Hospital Administrators; Hospital Design, Construction, and Equipment; Regional Planning of Hospital and Health Facilities; and Personnel Management. Further particulars may be had from Captain J. E. Stone, honorary secretary of the federation and congress, King Edward's Hospital Fund, 10, Old Jewry, London, E.C.2.

"Medical Press" Dinner

The 110th anniversary of the *Medical Press* was celebrated at a dinner in London on Jan. 26. Lord Moran, P.R.C.P., said that the founder and first editor, Arthur Jacob, P.R.C.S.I., with all his abundant interests, was first and foremost a reformer—one of the dangerous occupations. The task of a medical journal, Lord Moran thought, was to keep the profession up to date, to stir it up, and to educate it. To educate the public in medicine was more difficult, and perhaps the greatest advance in this direction was the use of the wireless. Sir Cecil Wakeley, the editor, said that the *Medical Press* had always been edited by men in clinical practice. It upheld the idea of a free press and free expression of opinion. Dr. Guy Dain, proposing Medical Journalism, said that the medical journalist was expected to have wide sympathies, a regard for accuracy, knowledge whether new work was important, tact in dealing with contributors, and a sense of responsibility to the public; and in these respects British medical journalism, though somewhat conservative, stood comparison with any other. Sir Heneage Ogilvie, editor of the *Practitioner*, said that Sir Cecil Wakeley had given the *Medical Press* a new lease of life. The medical journalist had to interest a critical and diverse public: his promises must be sober and must be kept. Mr. R. F. West, also responding, mentioned that the company included Mr. Robert Jacob, a great-grandson of the founder, and Mr. A. F. Tindall, lately retired after 52 years' work with the *Medical Press*. The founder, Arthur Jacob, like Wakley of the *Lancet*, had seen that reform was impossible without a forum for debate; both men had the temperament of Old Testament prophets, and their two journals did more to weld the profession into a homogeneous whole than any other influence of the time. Jacob believed in a free press to elicit truth, encourage honesty, and resist oppression. The most important function of the medical press today was still to maintain the unassailable right of the profession to express itself on every subject.

A Rest Home for Nurses

The trustees of the House of Rest, Buxton, Derbyshire, have given, to the Council for the Provision of Rest-Breaks Houses for Nurses and Midwives, Peveril House as a third rest-breaks house. All nurses and midwives, whether working or retired, in need of a rest-break or post-convalescence, will be eligible for admission. Applications should be sent to the warden, Peveril House, West Road, Buxton, Derbyshire.

National Insurance Contributions During Sickness

Employed and self-employed new entrants to the National Insurance Scheme on July 5, 1948, who were ill during the first six months of the scheme and, because they were not entitled to sickness benefit, did not notify the local National Insurance Office of their incapacity are advised to do so as soon as possible. This also applies to other people who were ill and for some reason did not wish to claim benefit. If the local office is notified of incapacity, contributions can sometimes be excused even though the insured person is not entitled to benefit. Until a contribution is excused, however, an insured person remains liable to pay a contribution for each week he is sick and not receiving benefit.

Dr. B. P. Watson, professor emeritus of obstetrics and gynecology in the Columbia University, New York, and a former professor of midwifery and diseases of women in the University of Edinburgh, has been elected president of the New York Academy of Medicine.

Diary of the Week

FEB. 6 TO 12

Monday, 7th

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, S.E.5
4.30 P.M.: Dr. G. L. Brown, F.R.S.: Transmission of Nervous Activity.

Tuesday, 8th

UNIVERSITY OF LONDON
5.15 P.M. (London School of Hygiene, Keppel Street, W.C.1.) Dr. Pierre Lépine (Paris): Virus Research and the Virus Problem.

UNIVERSITY COLLEGE, Gower Street, W.C.1
5.15 P.M. (Physiology theatre.) Dr. E. Ashworth Underwood: Integration of the Bodily Function. (Last of four lectures.)

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: Histopathology of the Skin.

CHELSEA CLINICAL SOCIETY
7 P.M. (South Kensington Hotel, 47, Queen's Gate Terrace, S.W.7.) Dr. Desmond MacManus: Insidious Onset of Grave Disease.

Wednesday, 9th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Sir Henry Cohen: Hypoglycæmia and Hyperinsulinism. (Moynihan lecture.)

ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St. Vincent Street, Glasgow
5 P.M. Dr. James Hutchison: Researches in Intrathoracic Tuberculosis in Childhood.

Thursday, 10th

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. Michael Oldfield: Advances in Hare-lip and Cleft-palate Surgery, following the Treatment of 500 Patients. (Hunterian lecture.)

UNIVERSITY OF LONDON
5 P.M. (Westminster Medical School, Horseferry Road, S.W.1.) Sir Hugh Cairns: Surgical Aspects of Meningitis.

INSTITUTE OF DERMATOLOGY
5 P.M. Dr. R. T. Brain: Physio- and Electro-therapy.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
11.15 A.M. Dr. T. S. Littler: Physical Principles of Audiometry and Hearing-aids.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, S.W.1
4.30 P.M. Neurology lecture-demonstration.

HONYMAN GILLESPIE LECTURE
5 P.M. (Edinburgh Royal Infirmary.) Dr. A. P. Meiklejohn: Diet and Dental Health.

Friday, 11th

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. K. F. W. Hinson: Pathology of Pneumoconiosis.

MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, W.9
5 P.M. Mr. W. S. McKenzie: Vestibular Diseases.

WEST KENT MEDICO-CHIRURGICAL SOCIETY
8.30 P.M. (Miller General Hospital, S.E.10.) Mr. J. Gabe. The Prostatic Patient.

Saturday, 12th

BIOCHEMICAL SOCIETY
11 A.M. (Westminster Medical School.) Symposium on Biochemical Aspects of Genetics.

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MEGALOCYTIC ANÆMIAS *

JOHN F. WILKINSON
M.D., M.Sc., Ph.D. Manc., F.R.C.P., F.R.I.C.

THE changes observed in the gastric mucosa of patients dying of pernicious anæmia led Flint (1860) to remark: "Nor is it difficult to see how fatal anæmia must follow an amount of degenerative disease reducing the amount of gastric juice so far that the assimilation of food is rendered wholly inadequate to the wants of the body." This observation, confirmed subsequently by Fenwick (1880) and many others, is singularly significant in the light of present knowledge of the ætiological factors in pernicious and other megalocytic anæmias. Equally important was the discovery of the absence of hydrochloric acid from the gastric secretion in pernicious anæmia, first mentioned by Cahn and von Mering (1886).

Some sixteen years ago I considered in detail the association of histamine-refractory achylia gastrica (with a deficiency of hydrochloric acid and pepsin) in pernicious anæmia, confirming its almost universal occurrence in that disease (Wilkinson 1932b, Blakely and Wilkinson 1933). Though some 80 cases have been described by various workers in which hydrochloric acid was found in the gastric secretion before treatment, most of these patients did not have true pernicious anæmia; in nearly all of them the marrow reaction was not indicated (bone-marrow biopsy was not then in use), and vital hæmatological evidence was absent. Of 9 patients of my own with megalocytic anæmia associated with free hydrochloric acid in the gastric juice 2 had megalocytic anæmias of pregnancy (Wilkinson 1932c); from further investigations of the remainder, only 3 (1 had only very slight amounts after histamine stimulation) appear to be true examples of pernicious anæmia, 1 has since been shown to have achrestic anæmia, and 3 do not conform to either of these diagnoses.

In my own consecutive series of 1600 cases of true unequivocal pernicious anæmia I have never seen a return of hydrochloric acid and pepsin after treatment with liver or stomach preparations or folic acid. However, 10 such cases have been reported, mostly on inadequate evidence, by Bloch (1903), Shaw (1926), Seyderhelm and Opitz (1928), McPeak and Neighbors (1928), Connery and Jolliffe (1931), Hurst (1930, 1932), Alsted (1934). The 2 cases of Campbell and Conybeare (1922, 1924) and Löwenberg and Gottheil (1928) had not had examinations before treatment. The general opinion now is to consider that these patients are really not true examples of pernicious anæmia; other cases reported were either devoid of hæmatological information or usually examples of other blood dyscrasias.

The passage of time and further experience have amply confirmed the necessity for finding a histamine-refractory achylia gastrica in such patients for a firm diagnosis of pernicious anæmia or subacute combined degeneration of the cord (Wilkinson and Oliver 1931, Israëls and Wilkinson 1936, 1940). The cause of this practically invariable association of achylia gastrica with pernicious anæmia has been fully considered (Wilkinson 1932b, Oliver and Wilkinson 1933), and there is much evidence to support the view that it is primarily a constitutional abnormality. In this connexion we recall the very common familial occurrence of achlorhydria or achylia with or without clinical symptoms (Wilkinson and Brockbank 1931).

From my own cases and from a few other adequately reported smaller series (excluding a few without any details) there have been at least 308 families in which two or more members had pernicious anæmia (siblings, or parents and children, forming the largest number), 75 families (with pernicious anæmia in one person) with achlorhydria in different members, and 27 families with achlorhydria in several members without anæmia. These last-named may be significant, since I have noted the frequent occurrence of hypochromic anæmia in other members of 78 of these families. In my own series 24% of all examined relations of patients with pernicious anæmia had achlorhydria or achylia, but many were entirely free of symptoms, and several undiagnosed quiescent cases of pernicious anæmia were discovered during our inquiries.

A deficiency in hydrochloric acid and pepsin, however, seems to be relatively less important than the absence of the anti-pernicious-anæmia principle normally found in the stomach and gastric juice. Unfortunately the method for its detection by clinical trial on patients with relapsing pernicious anæmia does not lend itself readily or conveniently to routine estimations.

DETERMINATION OF HÆMOPOIETIC POTENCY

Many tests of the hæmopoietic potency of anti-anæmic preparations of stomach and liver have been suggested, such as those based on changes in the numbers of reticulocytes or of erythrocytes in normal or in experimentally anæmic animals (dog, rat, guineapig, goat, pig, pigeons, and fish); other biological methods—e.g., tissue culture methods—and chemical, biochemical, and physical methods. Up to now none has withstood critical examination and direct comparison with the sole fairly reliable method—direct clinical trial on the controlled patient with pernicious anæmia. It is of the utmost importance that this clinical method should be rigidly controlled to avoid false interpretations and results, as I have often stated elsewhere (see Wilkinson 1932a, 1948). The main criteria are a patient with uncomplicated pernicious anæmia in relapse, with a red-cell count preferably below 2,000,000 per c.mm., achylia gastrica, and a typical megaloblastic hyperplasia of the marrow. The patient should be admitted to hospital for proper control during the test, liver and other offal should be omitted from the diet, and no effective prior treatment should have been given for at least seven days, to ensure that (1) the patient is not in a spontaneous remission; (2) the red-cell count and hæmoglobin percentage are not rising; and (3) the reticulocyte-count is constant and low (less than about 2%).

The response to treatment is obvious: with a hæmopoietically active preparation the number of reticulocytes begins to increase very rapidly, reaching a maximum in about 6–8 days, the peak being inversely proportional to the initial red-cell count. Thereafter the reticulocytosis diminishes, but the red-cell count and hæmoglobin percentage steadily and progressively return to normal, and the patient shows rapid clinical improvement. The megaloblastic marrow usually becomes completely normoblastic by the time of the maximal reticulocytosis. These changes are not seen if the preparation under test is inactive, and subpotent preparations may produce intermediate and less satisfactory results; in these cases subsequent treatment with known active preparations will demonstrate by further adequate responses that the patient was suitable for test purposes.

The Anti-anæmic Stomach Principle

Castle (1929) first showed that, whereas neither normal human gastric juice nor beef-muscle protein alone had any therapeutic effects when fed to patients with relapsing pernicious anæmia, when these were previously incubated together in vitro the mixture became hæmopoietically very active and induced complete remissions in such patients. Castle suggested that this represented the

* The Oliver-Sharpey lectures delivered at the Royal College of Physicians of London on March 9 and 11, 1948.

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interaction of an intrinsic stomach factor with an extrinsic factor in the food (or beef) to produce a hæmopoietically active substance, a failure of any of these leading to hyperchromic anæmia.

Wilkinson (1929, 1930) confirmed these observations and noted further that normal human gastric juice, though inactive when fed to patients with pernicious anæmia with empty stomachs, produced normal reticulocytosis and full remission when administered to patients who had been given protein (beef) food, without prior digestion, immediately beforehand.

It was an obvious step to try the effect of stomach tissue as a source of the active anti-pernicious-anæmia principle, and excellent hæmatological responses were obtained in the severest cases of pernicious anæmia by feeding minced raw, and (later) desiccated, pig's stomach, whereas sheep and ox stomachs were apparently inactive (Wilkinson 1929 and subsequent years).

The results were most encouraging and infinitely better than those then being obtained with liver, provided certain simple precautions were observed, for the hæmopoietic activity of the stomach preparation was destroyed if (1) it was heated at any stage above 45°C, (2) autolysis was allowed, especially in the presence of free hydrochloric acid, or (3) protracted digestion was permitted in the presence of pepsin and hydrochloric acid or trypsin (Wilkinson and Klein 1932).

These observations, which were so different from those seen with stable liver preparations, made it clear that the liver and stomach principles were not the same, the stomach principle behaving in its properties and action like an enzyme, similar to pepsin. The stomach principle was later termed hæmopoietin (Wilkinson 1930, 1931a and b, Wilkinson and Klein 1932). It was further shown (Klein and Wilkinson 1933) that hæmopoietically active thermostable extracts could be made from incubated hog's stomach by the methods used successfully to prepare potent liver extracts which are stable under the above conditions. Thus there were two anti-anæmic factors with different properties: a stable one present in liver, and a much more unstable one in stomach tissue.

Attempts to isolate the stomach principle have furnished more active products, but the identity of the enzyme hæmopoietin is not yet known. Hæmopoietin appears to be similar to, or identical with, Castle's intrinsic factor, and is not any known digestive enzyme, such as pepsin, rennin, kathepsin, and lipase, from which crude hæmopoietin can be separated easily in active form (Klein and Wilkinson 1933, Wilkinson and Klein 1933). These pepsin-free relatively crude preparations of hæmopoietin are dry, tasteless, and almost colourless powders capable of initiating remissions in pernicious anæmia in doses of 1–5 g. daily when given by mouth with meals but, as would be expected, they are inactive when given parenterally.

It was therefore believed that the clinical experiments with gastric juice, the necessity for an extrinsic substrate, the association of pernicious anæmia with deficient enzyme secretion (Wilkinson 1932a), the difficulty of extracting hæmopoietin from stomach tissue, its digestion by the protracted action of either of the proteolytic enzymes pepsin and trypsin, its association with the protein fraction of stomach press juice, its instability to heat, and its sensitiveness to chemical treatment all harmonised with the view that hæmopoietin was an organic substance of complex structure, probably an enzyme-like protein.

From a large series of oft-repeated incubation experiments with these stomach fractions containing hæmopoietin it was shown conclusively that crude hæmopoietin, given alone with meals or after incubation at 37°C with beef or beef myoglobulin, produced prompt reticulocytosis and clinical remissions in pernicious anæmia when given by mouth, but not if the hæmopoietin was heated to 60°C for half an hour before the incubation:

Hæmopoietic Potency of Incubation Products

Active

Hæmopoietin alone

Hæmopoietin + water + beef after incubation at 37°C

Hæmopoietin + water + beef after incubation at 37°C, then heated at 65°C for ½ hour

As above, then extracted as for liver extract

Inactive

Pepsin (HCl) alone

Beef + water

Beef + pepsin + water after incubation at 37°C

Hæmopoietin + water heated at 65°C for ½ hour

Hæmopoietin + water heated at 65°C for ½ hour, then incubated with beef at 37°C for ½ hour

On the other hand, the product from the incubation of hæmopoietin and beef at 37°C could be heated to 60°C for half an hour to destroy excess or unchanged hæmopoietin, and then worked up as for the extraction and preparation of a liver extract, which could be given intramuscularly or intravenously to produce complete hæmatological remissions in pernicious anæmia.

Thus we clearly demonstrated (and my successive biochemists have done so repeatedly) that the thermolabile hæmopoietin (the anti-pernicious-anæmia stomach principle or enzyme), which was only active when given by mouth, could be incubated with beef protein at 37°C and converted to a substance resembling, or identical with, the thermostable anti-pernicious-anæmia liver principle, active also on parenteral administration—i.e., there had been an in-vitro synthesis of the anti-pernicious-anæmia liver principle from the stomach enzyme hæmopoietin:

Enzyme		*Substrate*		*End-product*
Hæmopoietin	+	Beef protein	→	Active liver principle

The striking resemblance in properties and behaviour of the active liver principle and of the product formed in our incubation experiments appears to support their probable identity, differentiating them sharply from hæmopoietin:

Comparison of Anti-anæmic Principles

	Hæmopoietin	*Incubation product*	*Liver principle*
Precipitation with proteins	+	0	0
Protein reactions	+	0	0
Solubility in water	Soluble	Soluble	Soluble
Solubility in 70% alcohol	Insoluble	Soluble	Soluble
Solubility in 95% alcohol	Insoluble	Slightly soluble	Slightly soluble
Thermostability at 60°C	Rapidly inactivated	Stable	Stable
Thermostability at 100°C	Very rapidly inactivated	Slowly inactivated	Slowly inactivated
Incubation with beef at 37°C	Forms liver principle	Unchanged	Unchanged
Effects of acetone	Inactivated	Unaffected	Unaffected
Hæmopoietically active	Orally	Orally, parenterally	Orally, parenterally

These experiments all confirmed our views of the enzymic nature of hæmopoietin, the stomach anti-pernicious-anæmia principle which, I believe, is identical with Castle's intrinsic factor.

NATURE OF HÆMOPOIETIN

Ordinarily the commercial stomach preparations are made from selected parts of the pig's stomach or duodenum, desiccated and defatted, but a more active preparation is obtained by alcoholic precipitation of the crude hæmopoietin with pepsin from the stomach press juice, the pepsin then being removed by iso-electric precipitation (Wilkinson and Klein 1932, 1933). This forms a useful starting-point for experimental incubation and therapeutic work.

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Whether hæmopoietin is a proteolytic enzyme or not has not been determined with certainty owing to the difficulty of getting it pure enough and sufficiently free of pepsin and trypsin. It has been suggested that hæmopoietin is a prolinase or prolidase hydrolysing specific prolyl peptides (Mazza and Migliardi 1941), but Ågren (1944), starting from aqueous extracts of pig's pyloric mucosa, has claimed to have made active enzyme preparations containing an aminopolypeptidase which he thinks is identical with hæmopoietin. This has not been confirmed by Andersen and Faber (1946).

IS HÆMOPOIETIN A GASTRIC HORMONE?

An example of the fallacies that may arise if the nature and relationship of the stomach enzyme hæmopoietin and the liver principle are not clearly understood was the claim of Morris et al. (1932a and b) and Morris (1933) that gastric juice could be concentrated in vacuo and neutralised, and the product used to initiate reticulocytoses and remissions in pernicious anæmia; they considered that the active substance was a thermolabile dialysable exhaustible hormone. Their evidence and material were very poor and were severely criticised, particularly since the pig's "gastric juice" they used was apparently stomach contents obtained post mortem and therefore most certainly a mixture of hæmopoietin, extrinsic factor, and their incubation end-product, the liver principle (Wilkinson 1932d, 1933a). Our failure to confirm this work was supported by others.

It is of interest, however, in this connexion to note that we observed, as did Fouts et al. (1934), that concentration of gastric juice in vacuo might lead to the production of an ultrafilterable substance which produced reticulocytoses and remissions in pernicious anæmia when given parenterally. Apparently during the concentration the hæmopoietin reacts with an "extrinsic factor" in the gastric juice, producing a substance resembling the anti-pernicious-anæmia liver principle. This is not unexpected.

We found also that the influence of pepsin on hæmopoietic potency depended among other things on the duration and temperature of incubation and the pH of the solution. Greenspon (1936) suggested that pepsin in an acid medium inactivated hæmopoietin, and that the rôle of the extrinsic factor was to remove or inactivate pepsin, leaving the hæmopoietin fully potent alone without incubation; he said that a parenteral preparation of hæmopoietin could be made easily by cooling the gastric juice as soon as collected and then neutralising it. This work was not confirmed by us or by others—e.g., Castle and Ham (1936), Fitz-hugh and Creskoff (1936), Flood and West (1936), and Hanes et al. (1936). On the other hand, it is well known that toxic substances may be produced, under these conditions, which may cause protracted reticulocytosis without clinical remission.

SITE OF HÆMOPOIETIN SECRETION IN THE STOMACH

Experiments to identify the site of hæmopoietin production have been made by several groups of workers (Bence 1933, 1934, 1936, Fox and Castle 1942, Meulengracht 1934, 1935, 1936, 1939, Petri and Jensenius 1941, Petri et al. 1941, 1944, Wilkinson 1930, 1931a and b, 1933d, 1940, Wilkinson and Klein 1932, Wilkinson et al. 1938). It is now agreed that the potent areas in the pig are the pyloric region (the "pyloric gland organ" of Meulengracht). Less potent is the cardia, the fundus being inactive. In these areas the secretions of pepsin and rennin follow the reverse order, being small in the pylorus but considerable in the fundus.

Hæmopoietic activity is apparently not confined to the stomach in the pig, since active preparations have been made from duodenum (Gutzeit 1932, Meulengracht 1935, Sharp et al. 1931, Thompson 1937, Wilkinson 1931a and b), and Uotila (1936, 1938) has claimed that anti-anæmic potency is well marked in the jejunum and ileum, the latter being the greatest reservoir in the body; and Schemensky (1935) found some potency in the desiccated colon. Probably the activity claimed for the intestines may be due to adsorbed anti-anæmic principle in process of absorption and not secretion.

Nevertheless, there appears to be a wide distribution of anti-pernicious-anæmia potency in the pig's gastro-intestinal tract in the following order of decreasing potency: pylorus, ileum, duodenum, jejunum, cardia, colon, and fundus. With this extensive gastro-intestinal reservoir it is obvious that a megalocytic anæmia like pernicious anæmia would not ordinarily be expected to develop in pigs after total or partial gastrectomy (Bence 1934, 1936, Petri et al. 1941, 1944), and the Brunner's glands and pyloric glands may not be so specific in this respect as was originally suggested by Meulengracht (1935).

Numerous attempts have been made to produce typical pernicious anæmia in animals, particularly in dogs and pigs, by partial or total gastrectomies, but usually only a hypochromic anæmia, with or without pellagra, has been noted. Nevertheless, some rather inexplicable results have been obtained, mainly by Bence (1934, 1936), Goodman et al. (1935, 1936, 1937), and Petri et al. (1944), who have claimed that, some months after resection of the pig's (stomach) fundus, the liver becomes depleted of the anti-pernicious-anæmia principle; where only the fundus has been resected, nicotinic acid may prevent this, but most surprisingly it is not prevented by feeding 20 g. daily of desiccated pyloric mucosa for as long as four months. Despite the well-known observation that the pyloric gland organ has very active anti-pernicious-anæmia properties when given by mouth and is not inactivated by removal of the fundus, which possesses no hæmopoietic activity, Petri et al. (1944) suggest that the hæmopoietin in the pyloric-gland organ acts on the fundus, whose presence is essential for the normal formation of the anti-pernicious-anæmia liver principle by the hæmopoietin-extrinsic-factor reaction.

Landboe-Christensen and Bohn (1947) have shown that pig's duodenal juice collected from a pouch and fistula will produce hæmopoietic remissions in pernicious anæmia; they consider that this establishes a relationship between pernicious anæmia in man and anæmia produced in pigs by elimination of the duodenal secretion.

At Dr. W. Jacobson's suggestion we separated pig's duodenum into three fractions containing (1) villi and crypts of Lieberkühn (99%) and 1% of Brunner's glands; (2) Brunner's glands (66%) and 1–2% of villi and crypts; and (3) duodenal muscle layer. Fraction 1 (villi and crypts) gave good hæmopoietic remissions in test cases of pernicious anæmia, but fractions 2 and 3 were inactive. This result appears to support the idea that cells secreting the anti-pernicious-anæmia principle are present in this layer of intestinal mucosa and not in the Brunner's glands. But we have also shown that a thermostable extract can be made from the intestine different from the thermolabile hæmopoietin, a fact which supports the idea that the interaction of hæmopoietin with extrinsic factor produces a substance akin to, or identical with, the anti-pernicious-anæmia liver principle, which is absorbed via the intestinal mucosa, and it might explain the hæmopoietic activity of the intestinal fractions.

These results refer only to the pig's alimentary tract. As regards stomachs taken from other animals, whether given by mouth as desiccated preparations, or incubated with beef and given as a parenteral extract, I found that the ox, horse, and sheep did not furnish active preparations (Wilkinson 1933d). Stomachs obtained from carnivora—silver fox, lion, tiger, leopard, tigon, &c.—have given incubation products of fair or good potency when given by mouth or parenterally, but some of the weaker results may have been due to the old

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age of many of the animals. No or little hæmopoietic remissions could be induced with stomachs from sea-lions, or from herbivora—elephant, giraffe, rhinoceros, hippopotamus, bison, various deer, and other ungulates—or from amphibians and reptiles—giant monitors, crocodiles, alligators, lizards, and reptiles (both poisonous and non-poisonous) of various kinds.

The clinical results obtained with different portions of the pig's stomach did not seem to correspond with the pathological lesions found by Meulengracht (1937) and Magnus and Ungley (1938) in the stomachs of patients with pernicious anæmia—severe atrophy of the fundic region, with little alteration in the pylorus and duodenum.

From our examinations of separated portions (pylorus, fundus, and cardia) of human stomachs we found that the hæmopoietic potency, unlike what holds good in the pig's stomach, is present mainly in the fundus, less in the cardia, and not at all in the pyloric region. Similar observations were made by Fox and Castle (1942). These observations go a long way towards explaining the non-development of pernicious anæmia in patients after gastrectomy, since presumably at least some hæmopoietin-secreting glands are left in the cardiac region.

Now, it has been shown repeatedly that normal gastric juice and gastric juice from patients with conditions other than pernicious anæmia contain hæmopoietin (intrinsic factor). On the other hand, no patient with pernicious anæmia or subacute combined degeneration of the cord secretes or forms hydrochloric acid, pepsin, or hæmopoietin in the gastro-intestinal tract, whether in relapse or remission, even after years of adequate treatment (Wilkinson 1930 et seq.).

Similarly it has been shown conclusively (Wilkinson et al. 1938) that stomachs taken from normal people can be incubated with beef-muscle protein at 37°C (see above), subsequently heated at 60°C, and then extracted, in the same way that liver extracts are prepared, to yield parenteral preparations hæmopoietically active in the treatment of pernicious anæmia —i.e., the normal human stomach contains adequate hæmopoietin, even as the pig's stomach does.

On the other hand, similar preparations made from stomachs removed from fatal cases of pernicious anæmia or subacute combined degeneration of the cord, whether in relapse or remission at the time, were completely inactive when given in relapsing pernicious anæmia.

Human Stomachs

Hæmopoietically active		*Hæmopoietically inactive*
Normal subjects:	whole stomach	Normal subjects: pylorus
	fundus	Pernicious anæmia
	cardia	Subacute combined degeneration of cord
Achrestic anæmia		
Aplastic anæmia		
Polycythæmia		

We can conclude that the stomachs in patients with treated or untreated pernicious anæmia do not secrete detectable amounts of hæmopoietin, which is found in normal human stomachs or in those from pigs, silver foxes, and other carnivorous animals.

The irreversible nature of the gastric mucosal atrophy in pernicious anæmia had been generally accepted probably because the achylia gastrica, the most easily observed fault, was permanent. The results of gastroscopy of patients with pernicious anæmia, before and after treatment has produced full remission with normal blood-counts, have suggested that some cases show regeneration of the atrophic gastric mucosa (Jones et al. 1935, Schindler and Serby 1939a and b), though this has not been observed by others—e.g., Hartfall (1938). Magnus (1940) states that large areas of the atrophic mucosa of the fundus in pernicious anæmia are replaced, during remissions, by typical intestinal epithelium containing numerous Paneth and argentaffine cells at the bases of the crypts of Lieberkühn, contrary to Jacobson's (1939) statement that the argentaffine cells are absent from the alimentary tract in pernicious anæmia. When adequately treated, most cases of pernicious anæmia show relief and almost complete disappearance of symptoms, such as glossitis; hence it is perhaps not unexpected to find similar improvement in the gastric mucosa, though the secretory function may not return.

The Extrinsic Factor

The identity of the extrinsic factor or substrate, though widely investigated, is still unknown. Castle (1929) used first beef muscle and later a beef myoglobulin, but care is required in preparing the latter owing to the ease with which it is denatured (Jones et al. 1938). Other sources of the extrinsic-factor substrate have been described, including liver, stomach, muscle protein, and liver proteose (Reimann 1931, Helmer et al. 1933, Castle et al. 1944).

Strauss and Castle (1932) thought some member of the vitamin-B complex, such as lactoflavine, was the extrinsic factor, but this was not substantiated by others, such as Wills and Naish (1933) using egg-white extract, Lassen and Lassen (1934) yeast extracts rich in vitamins B_1 and B_2 complex, Diehl and Kühnau (1933) a purified preparation of vitamin-B_2 complex, and Ashford et al. (1936) pure lactoflavine incubated with gastric juice or with hæmopoietin. Extrinsic factor is present in wheat germ, rice polishings, eggs (Singer 1932), milk, probably tomatoes (Groen 1935, Miller and Rhoads 1934, Castle et al. 1944); and Davidson (1932), Goodall (1932), Wilkinson and Klein (1933), and Ungley (1933) obtained active results with autolysed yeast products alone without any incubation with gastric juice.

We have tried many other possible sources of extrinsic factor, which is widely distributed in protein foods, but beef myoglobulin, liver, and yeast remain the best sources of extrinsic factor for incubation experiments (Jones et al. 1938). None of the known members of the vitamin-B complex, either alone or in combination, can act as extrinsic factor (Castle et al. 1944). Recently it was thought that pteroylglutamic acid or the pteroyl hepta- or tri-glutamic acids might furnish more evidence along these lines, but the results of digestion or incubation with gastric juice or with hæmopoietin have not supported this hope. "Folic" acid is just as effective hæmopoietically without the influence of hæmopoietin, and potent sources of extrinsic factor as well as liver extracts may be completely devoid of folic acid or its conjugates.

The Liver Principle

Since the original report of Minot and Murphy (1926) on the treatment of pernicious anæmia with a liver diet, intensive work has been carried out on the nature and identity of the so-called anti-pernicious-anæmia liver principle. Liver extracts of increasing "purity" but of various degrees of potency have been made, but the essential nature of the liver principle still awaits elucidation. By various chemical and physicochemical methods products of less and less bulk and weight per unit of starting-material have been made, but the main effects appear to be the removal of gross impurities with variable degrees of inactivation, removal, or loss of the residual active principle; hence, it is a frequent and easy thing to end up with an extract of low or no hæmopoietic activity.

In our extensive investigations on the nature of the anti-anæmic liver principle it has been an ever-recurring problem that fractionations are rarely complete, and hæmopoietic potency can be found in more than one fraction. Thus large-scale purification of extracts leads to a well-marked loss of the anti-anæmic principle, which often may be thrown away in the "liver discards."

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Some years ago I examined some of these commercially discarded residues and filtrates and found significant amounts of potent anti-anæmic principle in them. A considerable number of reports have been published on the liver fractionations, and products have been made of which only a few mg. are needed for a therapeutic dose (Dakin and West 1935, Wilkinson 1936b; Laland and Klem 1936, Karrer et al. 1937, 1938, Emery and Hurran 1945, Emery and Parker 1946). The liver principle seems to be a polypeptide; but, since most of the highly purified liver fractions are still relatively crude, it is difficult to progress at other than a slow rate owing to the necessity for separating probably a mixture of polypeptides. The work is handicapped by the lack of a quick reliable laboratory test for the anti-pernicious-anæmia principle apart from the clinical test (Wilkinson 1932a).

From the therapeutic standpoint it is still a moot point whether this high degree of purification is an advantage, since some evidence has been offered in support of the view that there are a main or primary anti-pernicious-anæmia factor and at least three secondary or accessory factors, of which one is l-tyrosine, the others being a purine and a peptide (Subbarow and Jacobson 1936, Subbarow et al. 1935, 1936 a and b, Jacobson and Subbarow 1937, 1941). This has not been confirmed by other workers, but much clinical evidence supports the view that the highly purified liver extracts are not so efficient as the crude preparations in the routine treatment of pernicious anæmia and subacute combined degeneration of the cord.

The idea of multiple factors is intriguing, for I have often pointed out that preparations of liver and stomach may be obtained of which some will induce good reticulocyte reponses without subsequent clinical improvement or increase in the red cells and hæmoglobin, whereas others may produce good clinical and hæmopoietic responses without any significant reticulocytosis. Further, it is known that many substances, such as congo red, potassium arsenite, iron preparations, concentrated gastric juices, and other toxic substances, will produce a protracted reticulocytosis without further hæmopoietic response. Similar fallacies are encountered when Singer's rat test is used for the detection of hæmopoietic activity of various preparations. Thus, hydrochloric acid and pepsin or gastric juice from a patient with pernicious anæmia may cause reticulocytosis, whereas neutralised normal gastric juice or gastric juice from polycythæmia may not do so.

From another angle the occurrence of reticulocytosis raises interesting problems. It has been shown that there is present in liver extract a thermolabile reticulocyte-ripening substance which loses its activity after heating for 5 min. at 100°C (Jacobsen 1947). This principle, however, consists of two parts: a thermolabile fraction and a thermostable fraction identified as l-tyrosine. The thermostable fraction is said to be specific (Jacobsen and Plum 1942), though dioxyphenylalanine and hallachrom are clinically more potent in this respect (Gad et al. 1944). The thermolabile substance is present in other tissues, especially stomach, duodenum, and jejunum (Plum 1944, Bohn 1946).

From the reticulocyte-ripening fraction in gastric tissue a preparation containing xanthine was isolated but this was not so potent as leucopterin and folic acid; the last two however, were active without the need for l-tyrosine, which did enhance the effects if added, and were not inactivated by heat. The greatest concentration of the reticulocyte-ripening principle is in plasma, but this cannot be activated by l-tyrosine without previous treatment with acetone, since the thermolabile and thermostable fractions are linked together firmly. Plum (1947) states that there is a decrease in reticulocyte-ripening substances in the plasma of untreated pernicious anæmia and certain other conditions which can be corrected by giving l-tyrosine. Years ago, however, when trying to repeat Subbarow's work, I never obtained any hæmopoietic or clinical improvement after giving l-tyrosine with or without purine fractions to patients with pernicious anæmia.

HÆMOPOIETIC ACTIVITY OF MAMMALIAN LIVERS

The occurrence of an anti-pernicious-anæmia principle in mammalian livers that can be extracted and used in the treatment of human pernicious anæmia is particularly interesting in view of the failure to produce in animals an anæmia resembling pernicious anæmia.

Since relatively little was known about the occurrence of the anti-pernicious-anæmia principle in other species, I carried out an extensive series of investigations on the livers of mammals, birds, fish, and reptiles. The liver extracts were prepared in the usual way and were then subjected to clinical trial in relapsed cases of pernicious anæmia by parenteral administration. From our tests we have found that an active anti-pernicious-anæmia principle is present in the livers of a very wide variety of herbivorous, omnivorous, and carnivorous animals.

Hæmopoietically Active Livers

Herbivora	*Apes and monkeys*	*Omnivora*
Bison	Baboon	Man
Capybara	Chimpanzee	Pig
Cattle (ox and calf)	Drill	
Elephant	Gibbon	
		Carnivora
Giraffe	Green monkey	Leopard
Hippopotamus	Orang-utan	Lion
Horse	Red-faced Japanese monkey	Ocelet
Nilgai antelope	Rhesus monkey	Silver fox
Rhinoceros		Tiger
Sheep	*Fish*	Tigon
	Cod	
Marine Mammal	Halibut	
Whale	Salmon	

The best hæmatological responses were obtained with extracts of livers of herbivorous animals, such as calf, elephant, rhinoceros, hippopotamus, giraffe, horse, capybara, &c., and the omnivorous normal man and pig. Active preparations were also obtained from the livers of the lion, tiger, tigon, leopard, ocelet, and silver fox among others, but one lion liver with gross pathological changes and hepatitis did not give an active extract.

Whale liver yielded a very good hæmopoietic activity, but, surprisingly, two Californian sea-lions examined at different times did not furnish hæmopoietically active extracts—both were old animals, and one had a duodenal ulcer. Extracts of fish livers (cod, halibut, salmon, &c.) when freshly prepared were hæmopoietically active when given either parenterally or by mouth, but fish and whale liver discards or residues, after extraction of their oils with superheated steam, did not furnish active preparations at all.

Hæmopoietically Inactive Livers

Reptiles, Amphibia, &c.	*Mammals*
Alligator	Cattle with nakuruitis
Crocodile	Sea-lion
Giant monitor	Whale-liver residues
Anaconda	
Boa	*Fish*
Cobras (various)	Cod-liver residues
Pythons (rock) (royal) (Indian)	Halibut-liver residues

The livers from cold-blooded reptiles and amphibia were hæmopoietically inactive.

Some of the animals had been in captivity for many years, and others were recent or relatively recent importa-

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tions at the time of death; hence, though most of the livers were not obviously diseased, the stomachs may have had some degree of gastric functional atrophy which was usually not obvious at necropsy.

On the other hand, in experiments I have carried out over ten years ago, the livers from cattle dying of nakuruitis in Kenya Colony did not yield any semblance of a hæmopoietically active liver extract when tested on relapsed pernicious anæmia (fig. 1). The importance of realising that diseased or impaired livers may not yield hæmopoietically active liver extracts for the routine treatment of pernicious anæmia is obvious.

Since the introduction of food-rationing the sole commercial source of livers for the manufacture of British liver extracts in this country has been what are called "pharmaceutical" livers—i.e., livers rejected in the abattoirs as being unfit for human consumption owing to disease and pathological changes. Thus, only a variable proportion of the material may be actual liver tissue, and these livers certainly do not receive the best of treatment while awaiting disposal, a matter of vital importance if potent extracts are to be made. After some rough dissection these "pharmaceutical" livers become the starting-material for the preparation of commercial liver extracts.

As has been proved repeatedly, the best and most potent liver extracts are made from fresh livers that have been refrigerated or treated immediately after removal from the carcase, but these livers are now distributed for use as food. This must mean that the present-day liver extracts are less potent than they ought to be, and one can appreciate that toxic substances present or developing during autolysis before refrigeration may be extracted from these diseased livers. This is confirmed by the increased quantities of inactive total solids present in the final liver extracts, which in consequence may often be associated with a greater frequency of reactions and pain after injection into patients.

It has been my opinion during the last few years that British liver extracts are not so good or so potent as their corresponding pre-war preparations, and the starting-material ("pharmaceutical" liver) is certainly one reason for this. Such liver extracts will not be able to compete as an export to any country where fresh livers are available for the preparation of liver extracts.

This is illustrated by some comparative results taken at random from my records of patients treated with a 1937 liver extract and as nearly identical patients

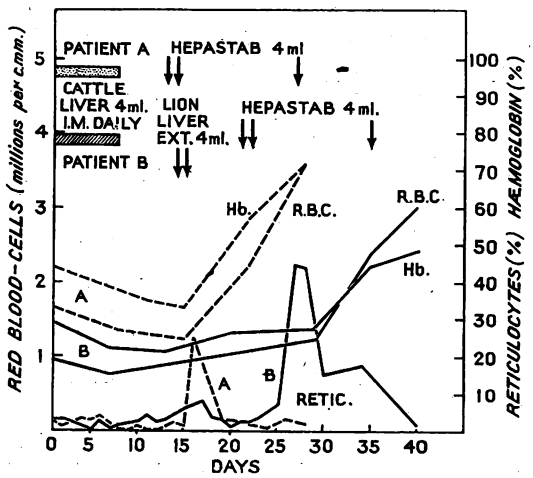

Fig. 1—Failure to initiate remissions in two patients (A and B) with pernicious anæmia after intramuscular administration of two different liver extracts prepared from cattle with nakuruitis, with subsequent good responses to ordinary commercial liver extract.

treated with a post-war (1945) liver extract of the same commercial brand and type given in the same dosage and prepared in the same way. The lower reticulocyte responses and the slower improvement in the red cells and hæmoglobin typical of a series of such cases are shown in fig. 2.

Further, the hæmopoietic potency of a liver extract is influenced not only by the poorness of the starting-material but also by the chemical processes used during extraction, all of which tend to reduce the hæmopoietic potency of the extract, since the liver principle is fairly easily destroyed or removed by many reagents used. Hence the absolute necessity for every batch, especially of the highly purified liver extracts, to be tested clinically before issue for general use. Unfortunately my experience is that this cannot be the universal vogue. I constantly see patients whose doctors have given them long or intensive courses of certain highly purified liver preparations with little or no clinical response, and then refer them as examples of liver-refractory pernicious anæmia when they are really examples of ordinary uncomplicated pernicious anæmia being treated with inactive liver extracts. (This applies particularly to the highly purified ones of the Dakin and West type.)

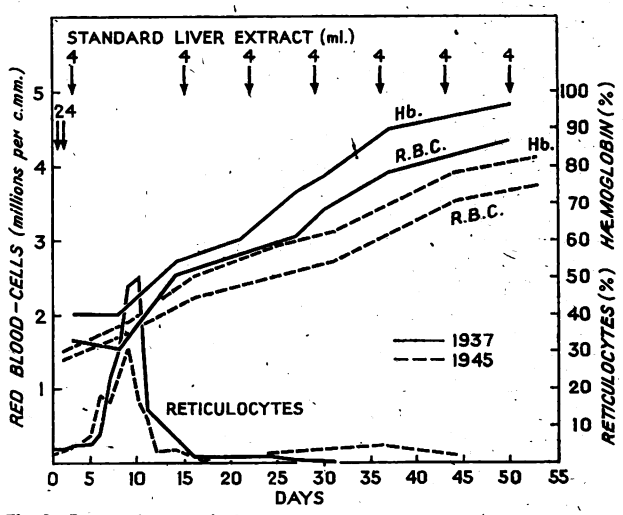

Fig. 2—Poorer hæmopoietic responses to post-war (1945) liver extract compared with responses to corresponding pre-war (1937) liver extract in patients as nearly identical and comparable as possible.

Wilkinson and Israëls (1947) have shown that a change to another but active intramuscular liver extract, or sometimes to another batch of the same brand, may reveal this fault (fig. 3).

There is much clinical and experimental evidence to suggest that the less highly purified preparations are better and more efficient in the treatment of pernicious anæmia and other megalocytic anæmias.

From a general consideration of the hæmopoietic processes it is important to remember that though anti-pernicious-anæmia liver preparations have been obtained from a very wide selection of mammals, birds, and fish, pernicious anæmia is unknown in any animals other than man, and attempts to produce it unequivocally in experimental animals by gastrectomy have been unsuccessful (Bence 1933, Ivy et al. 1931, 1934, Petri et al. 1944).

It is evident that our knowledge of the biochemical and physiological processes involved in normal hæmopoiesis and of the deficiencies leading to the various anæmias is far from complete.

HÆMOPOIETIC ACTIVITY OF HUMAN LIVER

The presence of a hæmopoietic principle in the liver of so many members of the animal kingdom naturally

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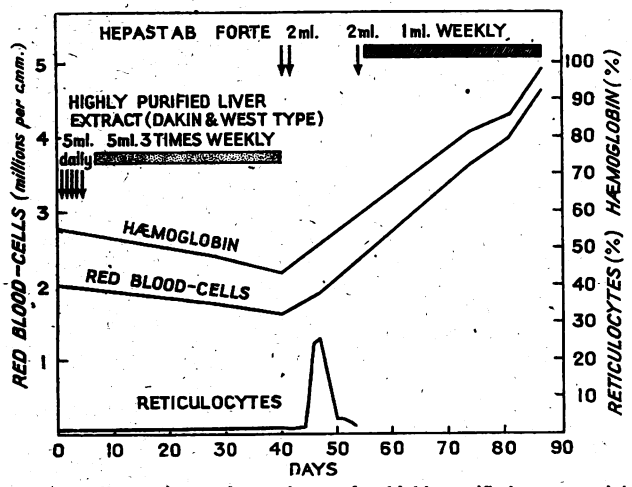

Fig. 3—Failure of very large doses of a highly purified commercial liver extract (Dakin and West type) to initiate remission in hospital-controlled patient with pernicious anæmia, who responded normally to less highly purified commercial liver extract of different type.

suggested that an examination of the activity of the human liver might throw some light on the problem of the megalocytic anæmias. With the hypothesis that hæmopoietin in the stomach acts on Castle's unknown extrinsic factor to yield ultimately the liver principle, which is stored in the liver, it was an interesting and necessary observation to determine the content of anti-pernicious-anæmia principle in the human liver in different conditions. As material became available, we investigated this point. The livers were extracted in the same manner as used in preparations of ordinary animal livers.

We showed that from clinical tests the human livers fell automatically into the following groups (Wilkinson and Klein 1934, Wilkinson et al. 1937):

(1) *Hæmopoietically Active*
- (*a*) Normal people
- (*b*) Polycythæmia
- (*c*) Aplastic anæmia
- (*d*) Achrestic anæmia
- (*e*) Liver cirrhosis
- (*f*) Pernicious anæmia in complete remission after treatment with stomach or liver preparations

(2) *Hæmopoietic Activity Diminished*
- (*a*) Pernicious anæmia after partial or inadequate treatment
- (*b*) Liver cirrhosis

(3) *Hæmopoietically Inactive*
- (*a*) Pernicious anæmia (untreated) in relapse
- (*b*) Subacute combined degeneration of the cord (untreated)
- (*c*) Liver cirrhosis

The anti-pernicious-anæmia potencies of liver extracts from normal people, aplastic anæmia, achrestic anæmia, and polycythæmia in group 1 were equal to those obtained from fresh calf liver. With these as standards, the liver extracts from patients with remitting pernicious anæmias who had had recent treatment and died of other causes were not quite so potent, suggesting that their livers contained much smaller amounts of the anti-pernicious-anæmia principle. In fact the amounts were directly proportional to the degree of remission or treatment given. On the other hand, the complete inactivity of the livers from relapsed pernicious anæmia (group 3) is in harmony with the view that pernicious anæmia is a deficiency disease and appears for the first time, or relapses, when the liver is depleted of its store of anti-pernicious-anæmia liver principle.

This may happen in several different circumstances —e.g., when there is a deficiency of extrinsic factor in the diet or an interference with the normal gastro-hæmopoietic mechanism. This latter would include (1) the absence of, or insufficient, hæmopoietin; (2) failure of the specific anti-anæmic gastric reaction; (3) failure of absorption from, or destruction in, the alimentary tract of the preformed anti-anæmic liver principle or any precursor—i.e., these factors exert effects at different stages of gastro-hæmopoiesis up to the actual storage in the liver (Wilkinson 1936a, Wilkinson and Klein 1934).

Other conditions may arise to interfere with the normal withdrawal of the liver principle from the liver depot and with its utilisation for normal erythropoiesis in the bone-marrow. The existence of such a condition was fully described by Israëls and Wilkinson (1936, 1940) under the name of achrestic anæmia—a megaloblastic anæmia with clinical features in general similar to those of pernicious anæmia (see below).

On the other hand, the ability of the liver to store the active principle may be diminished or lost in patients with hepatic cirrhosis, in whom the gastric secretion of hydrochloric acid, pepsin, and hæmopoietin may be normal.

In 1937 I suggested "the possibility of other as yet unidentified steps and mechanisms in the process of normal erythropoiesis has become more obvious. The manner in which the liver principle is mobilised from the liver and utilised in the further elaboration of the red cells is quite unknown, and there is no reason to assume that impairment of this stage is due entirely to toxic causes—there is some evidence to suggest that some of these cases may be the result of other deficiencies" (Wilkinson et al. 1937).

(To be continued)

PALLIATIVE SURGERY IN FACIAL PALSY

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THE facial palsy which results from irreparable damage to the seventh nerve is neither painful nor fatal but it is a serious deformity, humiliating to the patient, embarrassing to his friends, and, so far as the family doctor is concerned, intractable.

The problem of relieving these cases, though not hopeless, is complex; and many workers have attacked it from different angles. Important papers by Ballance and Duel (1932), Bentley and Hill (1936, 1940), Collier (1941), and Cawthorne (1942) were mainly concerned with suture, grafting, or anastomosis of the facial nerve; but it is not intended here to discuss this important aspect of facial palsy. My purpose is to review the suitability of tantalum wire as a supporting agent; to submit a preliminary report on a simplified fascial-sling technique; and, above all, to emphasise the relief which a carefully designed operation can give the unhappy patient.

WIRE SUPPORT

While surgeons were seeking a suitable material for a facial sling, which would be easy to handle, pliable, strong, and inert in a physical and a physiological sense, stainless steel and tantalum wire were naturally tried. Tantalum, which is not an alloy but an element, found some especially keen advocates; and it was buried in the face by various techniques, including open operation. The immediate results were often excellent; but, as Sheehan (1946) pointed out, experience with tantalum ribbon and wire was at that time insufficient to "pass on the manufacturer's claims that they are biologically inert." The favourable findings of the neurosurgeons with tantalum plates were not wholly applicable to another field, though the danger of electrolysis, even in the skull, was recognised by Lewin et al. (1948). Venable (1942) had previously described the nature of electrolysis.

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Briefly, any two metals (or alloys) of differing electrical potential, lying in fairly close proximity in the tissues, may act as a "destructive battery," with consequent corrosion. This will happen even though each of the two metals is "inert" if used alone. As nearly all adults have (or are likely to acquire) metallic dental fillings, which lie close to the cheek, the danger of inserting wires becomes obvious. Experience with these cases soon indicated that the risks were by no means only theoretical.

In this unit tantalum wire and stainless steel wire were given a short but intensive trial in 1946. We have not found a single case where fragmentation did not occur, involving both removal of the wire and the need for further surgery.

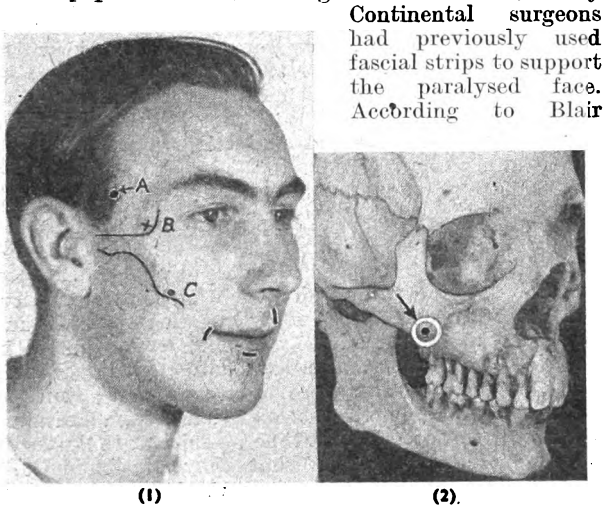
In one case tantalum and stainless steel wires were used in separate loops in the same cheek. Both wires fractured within six months, and on removal both showed corrosion, but the tantalum was more fragile than the stainless steel; here there were numerous metallic fillings in the adjacent teeth. In another instance tantalum wire, about 0·3 mm. in diameter, was inserted by a distinguished visiting surgeon, who also buried a lead plate in the upper eyelid. Within two months multiple fractures of the wire were seen on radiography. When the fragments were removed after four months the breaking-strain was only a few ounces as against about 8 lb. initially. The tissues in contact were stained black, and the wire was disintegrating. By contrast, the lead plate appeared unscathed, and the eyelid tissues were unstained.

It seems clear that two factors operate in these and many similar cases. First, dental fillings or other adjacent metals cause electrolytic action, with corrosion of the wire. Secondly, there is probably an alteration in the crystalline structure of the metal owing to continual stresses in the wire; passive facial movements, as in eating, would be sufficient to cause this.

The use of tantalum gauze in the cheek and lips has been advised by Schultz and Fowler (1947); while Douglas (1948), using gauze woven from wire of 0·075 mm. diameter, reported favourably on its behaviour both in experiments on animals and in the human abdominal wall. We have had no experience with this material, but it would presumably be subject to similar electrolytic action in the cheek, though it might disintegrate more slowly than wire.

ATTEMPTS AT ACTIVATION

Though Gallie and Le Mesurier did not publish their classic paper on fascia-lata grafts until 1921, many Continental surgeons had previously used fascial strips to support the paralysed face. According to Blair (1926) and other authorities, results had been published individually by Payr, Kirschner, Momberg, Busch, Stein, and Davis, between 1908 and 1913.



(1) (2)

Fig. 1—Position and direction of three incisions near mouth, and recommended point of proximal fixation (C) in relation to more distant alternative sites (A and B).
Fig. 2—Circle indicates site of drill hole at antero-inferior edge of malar bone.

Nevertheless, it was Blair himself who established the method, at least in Anglo-American circles, and contributed the one special instrument necessary to the procedure—the Blair "trocar-needle." A little later Gillies (1934), who had been a pioneer worker in this field since 1917, described an important refinement, the figure-of-eight loop of fascia embracing both upper and lower segments of the paralysed orbicularis oris muscle. He also advocated a temporal-muscle flap with fascia-lata attachment, to achieve active movements of the face; and he referred to the possibilities of transplanting part of the masseter, first performed by Eden, of Jena, in 1911. More recent papers include accounts of this latter operation by Adams (1946), and of the implantation of fascial strips through the masseter by Owens (1947).

Any "dynamic" operation which confers power of expression on a paralysed face must appeal strongly to both surgeon and patient. Apart, however, from great technical difficulties, there is a further and absolute disadvantage. The available muscles, the temporalis and masseter, are developed and adapted first for sucking and later for mastication. They are wholly devoted to this primitive biological function; and to misappropriate them, on the false analogy of successfully transplanting tendons in the hand, is open to criticism. It is therefore evident that difficulty may be expected in dissociating them from their established rôle and conditioning them to the subtle and largely involuntary movements of facial expression. This is precisely what has been found in practice. Most patients thus treated cannot avoid "making faces" while eating, and can hardly achieve easy or natural movements of expression. Spontaneity is a virtual impossibility.

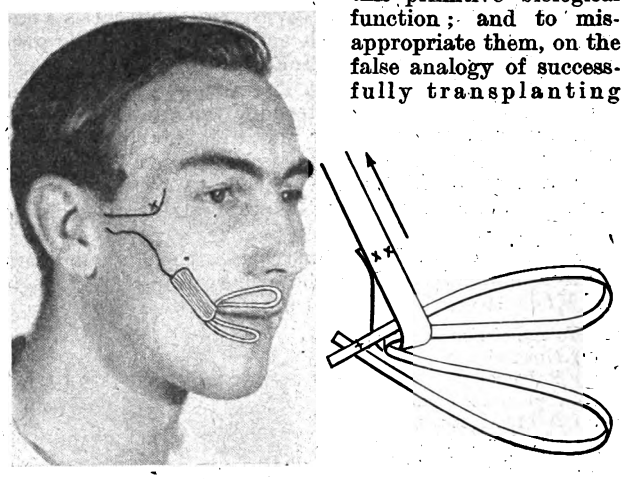


Fig. 3—Disposition of two fascial strips, showing "bite" obtained by figure-of-eight, direction of pull of broad sling, and relationship of slings.

A few patients, by dint of much practice in front of a mirror, do succeed; but their exaggerated efforts are a trifle grotesque and may even lead to a tic neurosis (A. H. McIndoe, personal communication). It may be as well, in passing, to repeat Gillies's warning that "before-and-after" photographs of these activated cases are unreliable.

STATIC SUPPORT

For these reasons it is felt that more can be gained by trying to improve the "static" type of operative support than by attempting activation with muscle transplants. As Sir Charles Ballance once put it, "those who are not Gillies might try a simpler method."

In seeking a better means of static support two points were recognised. First, the usual attachment of the

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(a) (b)

Fig. 4—Right facial palsy of 26 years' duration: (a) before operation, showing obliquity of mouth and deviation from midline even in repose; (b) soon after operation.

supporting slings to the temporal fascia could not be rigid; secondly, the length of each sling, about 5 in. (or 12·5 cm.), allowed a perceptible sag from early stretching during the phase of consolidation. A method designed to fix the proximal end of the fascia to bone and to reduce its length was sought. It was noted in dissections of the facial muscles that the most important muscle supporting the corner of the mouth is zygomaticus major, which arises from the malar. On these principles the following modified technique was recently adopted for adult cases.

Preoperative Splinting.—To minimise the early post-operative drag it is important to fit a temporary and detachable intra-oral wire hook, which will support the corner of the mouth. This is carried either on cap splints fitted to the upper premolars or, in edentulous patients, fixed to the upper denture. It can be adjusted for comfort in the days immediately before operation, detached during the operation, and replaced at its conclusion. Such a device, fitted as soon as possible after the original injury to the facial nerve, will do much to prevent serious sagging. In transient or incomplete lesions it will hasten recovery.

Operation.—The usual three tiny incisions (fig. 1) are made round the paralysed side of the mouth, and a strip of fascia lata 8 in. × 1/4 in. (20 cm. × 0·6 cm.) is inserted with a Blair needle in the Gillies figure-of-eight. The two ends, brought out of the lateral incision, are sutured together with silk.

The end of a second strip, 3 in. × 5/8 in. (7·5 cm. × 1·5 cm.), is taken round the double loop already formed at the corner of the mouth, and sutured to itself. An open approach to the fascia lata is preferred, since this allows of greater exactitude in taking the grafts from the strongest part of the iliotibial tract. A further incision 1 in. (2·5 cm.) long is now made over the anterior end of the lower free border of the malar bone, which is cleared sufficiently to allow a 3 mm. hole to be drilled near its edge (fig. 2). The free end of the wide strip is now drawn subcutaneously up to the malar incision, brought through the hole in the bone from back to front, and sutured both to the periosteum and to itself. Silk or 40 s.w.g. stainless steel wire may be used (fig. 3). When folded, the wide strip fits the hole closely.

It is important to "take the strain" with great care before the final fixation is done, and overcorrection is essential. This may be roughly expressed as lifting the corner of the mouth 1/4 in. (0·6 cm.) higher than the desired level. Closure of the four incisions and the firm application of a crêpe bandage complete the operation.

DISCUSSION

The mean length of the sling from mouth to malar bone is 1 3/4 in. (4·4 cm.). From mouth to zygomatic arch is about twice this distance, and from mouth to temporal fascia three times (fig. 1). Hence the sag, due to stretch—which must vary directly with the length of the sling—is greatly reduced. There is, however, always a tendency for the figure-of-eight to slacken in spite of a bite that includes unparalysed portions of the orbicularis oris muscle. The hole in the malar bone is easily made with a dental drill, and the alternative dissection round the zygomatic arch is avoided. There are no skin flaps to reflect, and no extensive undermining; thus the chance of a large hæmatoma forming, and therefore the risk of sepsis, is reduced to a minimum. No infection has occurred in any of the seven cases treated up to now by this technique. Asepsis is further assured by care in preventing contact between the graft and the surrounding skin.

The three tiny scars near the mouth are virtually imperceptible in a few weeks. The same is true of the malar incision, always provided it is planned to lie exactly in the line of skin tension. This is not a standard direction, and must be defined precisely in each case.

In spite of criticism directed against its clumsy appearance, the Blair fascia needle remains the best instrument for its purpose. Other methods, such as the use of a wire snare carried on a dental awl, are more damaging. It is, however, essential to pass the needle with great care and under the strictest control; the facial muscles are atrophic, and there is only a shallow plane between the sweat-glands in the skin and the mucous glands on the buccal surface. These offer a likely portal of entry for infecting organisms, if the fascia is too superficially or too deeply placed. A relatively wide sling is important, since strength is thus assured; also it does not tend to produce a ridge in the overlying skin of the cheek.

As regards results, the patients have all been highly gratified, but this has been observed after any well-designed operative support. They have been quick to note the complete relief from dribbling and from feeling (as well as looking) lopsided (fig. 4). The surgeon, on the other hand, if he maintains an objective attitude, must always realise that he has not achieved a "cure" but only mitigated a disaster, itself often of surgical origin.

Epiphora is a variable symptom, and it is usually lessened by this type of operation, which simply eases the drag of the flaccid cheek on the lower lid. Yet a method of attack on this problem must be part of a logical plan, since there are cases where epiphora is the principal symptom. It is hoped in due course to offer a tentative solution which will be complementary to the operation here described.

This preliminary presentation of a very small number of cases, treated in nine months by a modified technique, may appear premature. But the results have been so encouraging to all concerned that it was decided to submit an early report, in the hope that others will give the method a more extensive clinical trial.

SUMMARY

Unilateral facial palsy, unless merely transient, is a grave disability.

Brilliant results have been achieved by nerve repair, but many cases are unsuitable for this.

Palliative operations to support the face depend on the use of a suitable material.

Stainless steel and tantalum have been widely used and warmly advocated as reliable and inert.

Instances of failure are described which are attributed to electrolytic corrosion by other metals and to alterations in crystalline structure.

The use of wire slings in the face is not recommended.

The history of the development of fascial grafts to the face is reviewed, and reasons are given for the failure of activation by muscle flaps.

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A short broad fascial sling with rigid proximal fixation offers advantages of simplicity and security.

A modified technique, involving attachment to the malar bone, is suggested.

I am indebted to Sir Archibald McIndoe for constant encouragement; to my dental colleagues, particularly Mr. T. G. Ward, for advice and coöperation; and to Mr. Clemetson for the photographs.

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BENADRYL IN THE TREATMENT OF PARKINSONISM

RESULTS IN FORTY CASES

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James Parkinson, in the preface to his *Essay on the Shaking Palsy*, 1817, "considered it to be a duty to submit his opinions to the examination of others, even in their present state of immaturity and imperfection." Encouraged by these words, we describe here our experience of the treatment of parkinsonism with 'Benadryl.'

In April, 1947, a patient with advanced parkinsonism, who was bedridden owing to extreme rigidity and had not responded satisfactorily to classical treatment, was put on benadryl. The result was so dramatic that search was made for similar cases. A second patient with much rigidity was started on treatment a month later, and the series now includes forty cases.

CASE-RECORDS

Case 1.—A man, aged 61, had had parkinsonism for four years. There was no previous history of encephalitis. The patient had a typical parkinsonian appearance, pill-rolling tremor of both hands, and slow and difficult speech, and could not dress himself. His movements were extremely slow; he took about 10 sec. to turn through 90°. Under treatment with tinct. stramonii his condition had gradually deteriorated until November, 1946, when he was confined to his house and ultimately became bedridden with extreme generalised rigidity, unable to turn over in bed or to feed himself without assistance.

In June, 1947, he was given benadryl 50 mg. t.d.s. After 7 days he could move round in bed, and within 3 weeks he left his bed, able to walk, dress, and feed himself. In July, 1947, he was admitted to hospital for an unrelated condition, and treatment with benadryl was stopped. This caused a complete relapse within 48 hours. A few days after his discharge from hospital benadryl was given again with beneficial result. This dosage has been maintained for the past 18 months, and the initial improvement has been sustained. There has been no sign of toxic reaction to benadryl.

Case 2.—A woman, aged 46, with mask-like facies, no ocular accommodation-convergence reflex, slight external strabismus, fundi normal, cog-wheel rigidity of arms and legs, tremor of arms, deep reflexes present and equal, plantar reflexes flexor, sensation normal, other systems normal, and blood-pressure 120/80 mm. Hg. Severe cramp in the calf muscles seldom allowed her an uninterrupted night's rest. She could not walk without falling to the right, occasionally injuring herself. She had already received the classical forms of treatment but abandoned them because of intolerable side-effects. She had been in this condition for about two years.

At midday on July 18, 1947, she was given benadryl 50 mg. and told to take this dose three times a day. By the evening of the same day she had gained control over the tremor of the arms and the cramp had disappeared. Three days later her supply of benadryl was exhausted, and within 48 hours the condition had completely relapsed. Five days later she was re-started on 50 mg. four times a day, and again, within a few hours, the effect was well marked. She could rise from the sitting position without assistance and walk about the house without the tendency to fall to the right. The cramp in the legs had again disappeared. Fourteen days later she went by taxi to the opera. On Aug. 15, 1947, she was tried on an inert substance. Complete relapse occurred, and benadryl was again prescribed. Even under full treatment she remains an unmistakable case of parkinsonism but can do her housework and carry on her own correspondence.

SUBSEQUENT EXPERIENCE

When it became evident that this form of treatment might be of lasting benefit in parkinsonian rigidity, the series was extended to 40 cases chosen at random, with the object of analysing the therapeutic effect of benadryl on the other manifestations of parkinsonism. Analysis of the clinical results of treatment of these cases has shown that there are limitations to this therapy.

Rigidity is consistently improved. The relaxation achieved is accompanied by improvement in spontaneous movement, in the gait, and in the clarity of speech. Three patients thus benefited can undertake light work after a period of unemployment lasting two years or more. All the patients with rigidity previously unable to wash and dress themselves can now do so. The improvement in speech is one of the objective manifestations most easily assessed. Before treatment it was extremely difficult to obtain a history because of this disability in some of the cases. The contrast when they subsequently attended this clinic was most striking. It is questionable whether the relaxation obtained is the sole cause of the improvement in these other features, or whether an as yet undetermined therapeutic effect is responsible.

Tremor responds on the whole poorly. In early cases, in which tremor is limited to one part—e.g., one limb—there is considerable improvement. Two female patients, who, before the treatment, could not cut bread because of shaking of the right hand, overcame this disability in seven days. A male patient, who previously had to steady his arm with the unaffected hand while writing, can now dispense with this aid. But in most cases, especially where the tremor is at all severe, or is generalised, no benefit is obtained.

Akinesia, when unaccompanied by rigidity, is invariably aggravated.

Oculogyric crises do not respond. There is one exception in the series, in which this manifestation has been in abeyance since treatment was started three months ago.

Muscular cramp is abolished within a few hours of starting treatment.

ADMINISTRATION OF BENADRYL

The best results are achieved by giving benadryl 50 mg. three or four times daily. Within 10 days the therapeutic effect reaches its maximum. Thereafter increase in dosage cannot be expected to produce any further improvement. Physiotherapy and rehabilitation exercises are useful when the greatest relaxation has been attained.

Benadryl can be used in conjunction with the classical forms of treatment. When it is intended to treat with benadryl a patient already receiving belladonna, it is most unwise to stop the latter suddenly. In postencephalitic parkinsonism sudden withdrawal of the patient's usual medicine may lead to a severe oculogyric crisis, which

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will prejudice him against the new treatment. It is therefore better to wait for two weeks after starting benadryl before weaning the patient from a mixture which has been causing undesirable side-effects.

Benadryl does not cure; its effect is purely palliative, and complete relapse occurs within 48 hours of withdrawal.

SIDE-EFFECTS

Benadryl is free from the unpleasant side-effects characteristic of the classical forms of treatment—dryness of the mouth and paralysis of accommodation. In about a third of the series benadryl caused somnolence for the first 14 days or so of the treatment. This was in no case serious and was easily counteracted with amphetamine 5 mg. in the morning. Sudden withdrawal of benadryl produces no symptoms and is not dangerous.

TOXICITY

No case in this series showed any toxic effect. Two of the patients have now taken 200 mg. daily for over 18 months without any ill effect. In no case has there been a significant change in the blood picture.

All but four of the patients had previously received, in some cases for several years, the classical routine treatment for parkinsonism. It therefore seemed unlikely that they would be influenced unduly by the enthusiasm with which this new treatment was given. However, to overcome this possibility, use was made of dummy capsules, identical in appearance with the genuine article. In every successful case in which the dummies were substituted for benadryl without the patient's knowledge complete relapse occurred.

COMMENTS

It is interesting to compare these results with the findings of Sigwald and his colleagues[1] with another anti-histamine drug, diethylaminoethyl-N-thiodiphenylamine ('2987 R.P.'). They treated 30 cases, and obtained 7 very good results, 16 good results, and 5 partial failures. Of the 2 failures, one was due to complete intolerance, and the other patient was discovered later not to have been taking the drug. They obtained the same good results in rigidity and its associated manifestations. Slight tremor ceased completely and violent tremor was modified. Oculogyric attacks gave variable results. As with benadryl, the patient remained unmistakably the victim of parkinsonism, and withdrawal of the drug led to relapse. Budnitz,[2] in America, records the results of treating 8 cases of parkinsonism with benadryl.

SUMMARY

The results of treating 40 cases of parkinsonism with benadryl for more than a year suggest that this drug is most useful in this condition, and that it lacks the side-effects of the atropine group of drugs. The treatment is simple, and laboratory control seems to be unnecessary.

We wish to thank Dr. E. T. Baker Bates, Dr. R. W. Brookfield, Sir Henry Dale, and Dr. R. R. Hughes for their help in this investigation, and Dr. J. Stanley White, of Messrs. Parke, Davis and Co., for making and supplying the inert control capsules.

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"... Most of us, by being civilised too early or too forcibly, have been driven to believe that our natural human urges are 'bad,' 'not nice,' 'wicked,' 'sinful,' or whatever the local equivalent may be. This is the dreadfully damaging concept of 'original sin,' which really only states that babies are not born civilised according to the local customs of the natives."—Dr. G. BROCK CHISHOLM, *Science*, Jan. 14, p. 27.

ACUTE OSTEOMYELITIS DUE TO A PENICILLINASE-PRODUCING STAPHYLOCOCCUS AUREUS

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EVER since it was shown that some strains of *Staph. aureus* were resistant to penicillin, it has been anticipated that cases of acute primary hæmatogenous osteomyelitis due to such organisms would be described. Such infections are rare, but the following list of reported cases includes two of infection with strains of *Staph. aureus* four times as resistant as the Oxford staphylococcus (McAdam 1945, Agerholm and Trueta 1946):

Reporters	*Cases of acute hæmatogenous osteomyelitis stated to be due to Staph. aureus*	*Penicillin-resistant strains*
Altemeier and Helmsworth (1945)	29	None
McAdam (1945) ..	35	One strain four times as resistant as Oxford staphylococcus
Agerholm and Trueta (1946)	25	None in series, but one strain referred to in text which was four times as resistant as Oxford staphylococcus
Higgins et al. (1947) ..	13	None
Dennison (1948) ..	33	None
Tucker and Hollenberg (1948)	28	No note of any resistant case
Unpublished cases 1946–48 (C. C. J.)	12	One strain twice as resistant as Oxford staphylococcus

There was no mention of the production of penicillinase by any of the staphylococci isolated. However, it is now well known that penicillinase is produced by most of the naturally occurring penicillin-resistant strains of *Staph. aureus* (Bondi and Dietz 1948), and that the activity of penicillinase reduces the clinical value of penicillin. The degree of reduction has yet to be defined.

We report here a case of acute hæmatogenous osteomyelitis due to such a penicillinase-producing *Staph. aureus* in which penicillin therapy failed clinically.

CASE-RECORD

A boy, aged 12 years, had twisted his left ankle while playing cricket on May 30, 1948. Next day he reported at the Birmingham Accident Hospital with a painful ankle, but no abnormality was detected by radiography. On June 1 he reported again, complaining of severe pain in the ankle.

On examination (C. C. J.) he looked feverish, with tongue and mouth dry, small septic abrasions on both legs, temperature 100·8°F, and pulse-rate 108 per min. There was a definite increase of local heat above the left ankle, with extreme tenderness over the lower end of the tibia. There was no redness, and very little swelling. Ankle movements were painful towards the end of the range. A blood-culture remained sterile for 14 days. White-cell count 15,300 per c.mm. (polymorphs 76·5%). Acute osteomyelitis of the lower end of the left tibia was diagnosed, and the boy was admitted to hospital.

Treatment.—Intramuscular penicillin, 30,000 units 3-hourly, was begun on June 1. By June 3, there being no improvement in the local condition of the leg, the dosage of penicillin was raised to 60,000 units 3-hourly.

First Operation (C. C. J.).—On June 5 increased swelling and exquisite tenderness were noted at the lower end of the tibia. Under general anæsthesia a posterior subperiosteal abscess at the lower end of the tibia was drained. Pus was mopped away, and the wound was sutured. A small rubber tube was inserted to permit twice daily local therapy with

* In receipt of a part-time grant from the Medical Research Council.

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penicillin 30,000 units. The pus yielded a pure culture of an active penicillinase-producing *Staph. aureus* more than 1200 times as resistant as the Oxford staphylococcus (see below).

Progress.—On June 8 there were signs of spread of the inflammatory process to the upper two-thirds of the tibia, with a large subperiosteal abscess in this region. The dosage of penicillin was raised to 125,000 units 3-hourly. Serum-penicillin estimation then showed a bactericidal titre of 1 : 4 to 1 : 8 against the Oxford staphylococcus. 'Sulphamezathine' therapy was started.

Second Operation (C. C. J.).—On June 8, under general anæsthesia, the old incision was reopened, but very little pus was found. The lower part of the shaft of the tibia was drilled, but no pus was found. A fresh incision was made to drain a very large subperiosteal abscess in the upper two-thirds of the tibia. Pus was mopped away. Both wounds were left open and dressed with tulle gras, gauze, and a long leg plaster.

Streptomycin Therapy.—In view of the report of a positive blood-culture taken on June 8 and the continued lack of clinical response, alternative chemotherapy was considered. Streptomycin was selected because of the in-vitro sensitivity of the staphylococcus isolated to a concentration of streptomycin that should be obtainable in the blood. From June 10 it was given intramuscularly 6-hourly in the dosage recorded in fig. 1. Penicillin was discontinued after 6,000,000 units had been given in 9 days. Sulphamezathine also was discontinued because of reported clinical failures, notwithstanding an in-vitro sensitivity of the staphylococcus isolated to 5 mg. per ml. A total dosage of 10·5 g. had been given in 3 days.

Progress.—During 28 days' streptomycin therapy (total 38·5 g.) the temperature and pulse-rate gradually subsided, though they never remained within normal limits. Radiography showed extensive disease of the bone (fig. 2).

Ten weeks after the onset of the disease the general condition was satisfactory. For the first time the temperature had remained below 99°F for 7 consecutive days. There was no swelling of the leg or any sign of acute inflammation. At the centre of each operation wound was a sinus surrounded by exuberant granulations about 1 cm. in diameter. Both sinuses were swabbed. Cultures yielded a few penicillinase-producing *Staph. aureus*. No other organism was isolated.

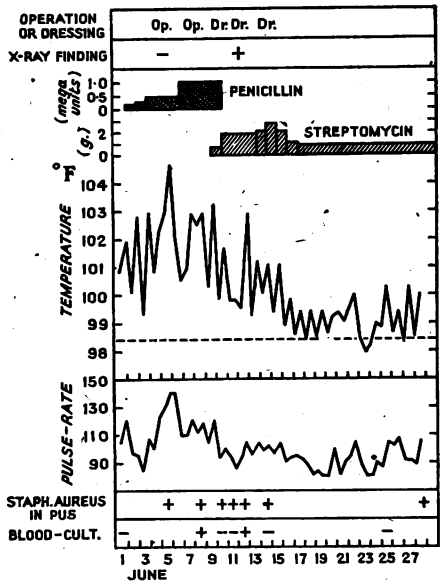

Fig. 1—Clinical chart of a case of acute osteomyelitis in which temperature and bacteræmia did not respond to 9 days' penicillin therapy.

Condition 5 months after Onset.—An operation had been performed to remove multiple large sequestra. The clinical condition had become chronic. Numerous sinuses were present. Penicillinase-producing *Staph. aureus* were still isolated at each dressing.

LABORATORY FINDINGS

Bacteriology.—The blood-culture (fig. 1) was positive twice. The *Staph. aureus* † isolated was not typable with any of the available phages. It had the same order of resistance to penicillin, sulphonamides, and streptomycin as the *Staph. aureus* isolated on the same days from the subperiosteal pus. It actively produced penicillinase.

The subperiosteal pus yielded on every occasion (fig. 1) from the 5th to the 65th day of disease a culture of penicillinase-producing *Staph. aureus* which was not typable by phage. No other pathogen was isolated, and in all but one instance the staphylococcus was in pure culture.

No attempt was made to measure quantitatively the rate of production of penicillinase. All strains completely destroyed penicillin when a 24-hour broth culture was incubated with about 30 units per ml. for 3 hours followed by overnight cylinder assay. The indirect evidence that the organisms actively produced penicillinase rests, first, on the unusually wide zone of penicillin inhibition when the organisms were plated on solid media containing penicillin, and secondly, on the great increase in penicillin resistance with increasing size of inoculum. In serial broth dilution tests the *Staph. aureus* was resistant to 200 units per ml. (× 10,000 the Oxford staphylococcus) when there was a final concentration of about 1,000,000 organisms per ml., but was resistant to only 0·2 unit per ml. when 1000 organisms per ml. were used. Similar differences between small (10–50 colonies) and large inocula were demonstrated on solid media containing different concentrations of penicillin. There was no significant variation in resistance either during or after penicillin therapy.

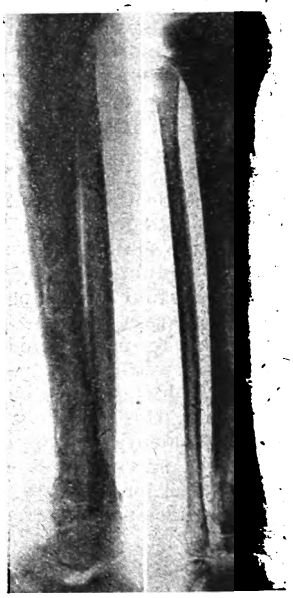

Fig. 2—Radiograms taken on 29th day of disease, showing extensive involvement of bone (same case as fig. 1).

The *Staph. aureus* was always sensitive to 5 mg. of sulphonamides per ml. and sometimes to 1 mg. per ml. It was sensitive to 0·01 mg. of dibromopropamidine per ml. (Wein et al. 1948). It did not vary in its sensitivity to streptomycin, and was of the same order of sensitivity as the standard strain of Friedländer's bacillus (K41, sensitive to 0·16 unit of streptomycin per ml.).

The blood-streptomycin levels were of the order expected with the prescribed dosage. For example, an hour after the administration of streptomycin 0·5 g. the serum-streptomycin level was 40 units per ml., and 5 hours later it was 0·2 unit per ml. (1 unit = 1 μg.).

Urine.—On many occasions from the 15th to the 49th day of the disease, a few hyaline and granular casts were present. They were absent from all earlier and later specimens. There was never any albuminuria. The blood-urea level remained normal.

Blood.—The white-cell count varied from 15,600 to 5900 per c.mm. Differential counts showed no abnormality apart from polymorph leucocytosis. Some degree of anæmia (Hb 85%, red cells 3,890,000 per c.mm.) had developed by the 7th week, but the blood was returning to normal (Hb 92%) 3 weeks later. The blood-platelet level (repeatedly tested during streptomycin therapy) never deviated from normal.

DISCUSSION

The clinical course of this case, treated early with penicillin, may be contrasted with the progress of similarly

† By *Staph. aureus* we mean a coagulase-positive gram-positive coccus.

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treated cases reported by other workers. That penicillin therapy failed in this case is shown by the following evidence:

(1) Persistent elevation of temperature and pulse-rate even after an adequate evacuation of a subperiosteal abscess on the 4th day of penicillin treatment (cf. Agerholm and Trueta 1946, Altemeier and Helmsworth 1945).

(2) Local spread of the inflammation during penicillin treatment, with the result that on the 7th day of penicillin treatment an even larger subperiosteal abscess higher up the tibia had to be drained.

(3) Positive blood-culture on the 7th day of penicillin treatment (cf. Aird 1945, McAdam 1945, Higgins et al. 1947, Dennison 1948).

(4) Positive wound culture up to the 65th day of the disease (cf. McAdam 1945).

The effect of streptomycin therapy has been difficult to assess. The impression is that the result has been less satisfactory than would have been expected in a similar case due to a penicillin-sensitive organism and treated with penicillin from the 10th day of the disease (the day streptomycin was started). This impression is based on the incomplete settling of temperature and pulse-rate after 28 days' therapy, the failure of the drainage wounds to heal, and the persistence in them of the causal organism. Bacteræmia, however, was controlled, but whether this was due to the effect of the drug or to the patient's natural resources cannot be told.

The findings in this case support the hypothesis that in the presence of penicillinase-producing *Staph. aureus* penicillin therapy is unlikely to be effective. However, the possibility has not yet been excluded that massive penicillin therapy might succeed where the routine dosage fails. In the present case the theoretical requirement based on in-vitro tests was a continuous serum-penicillin level of 1000 units per ml. King et al. (1947) have obtained continuous serum-penicillin levels of over 100 units per ml. by continuous intravenous infusion of 1,000,000 units per hour, combined with 'Caronamide' by mouth to suppress renal excretion of penicillin. In the absence of alternative chemotherapy, such as streptomycin, massive penicillin therapy might be considered.

These alternatives in therapy make it important to know as early as possible the penicillinase production as well as the penicillin sensitivity of the pathogen. Blood-cultures should be taken early, and repeated if the clinical condition does not improve. The early recovery of organisms from the bone lesion may be facilitated by such measures as early marrow culture or early bone drilling—proceedings recommended for diagnosis and treatment by some surgeons (Aird 1945, McAdam 1945, Agerholm and Trueta 1946, Tucker and Hollenberg 1948).

SUMMARY

In a case of acute primary hæmatogenous osteomyelitis due to a penicillinase-producing *Staph. aureus*, early penicillin therapy was not effective.

Streptomycin was given from the 10th day of the disease. There is insufficient evidence to say whether this therapy altered the clinical course.

Further trials of the chemotherapy of osteomyelitis due to penicillinase-producing *Staph. aureus* are required.

Early and complete bacteriological diagnosis is essential.

Our thanks are due to Dr. A. L. P. Peeney, clinical pathologist of the Queen Elizabeth Hospital, for advice on the control of streptomycin therapy; Dr. V. D. Allison, of the Central Public Health Laboratory, Colindale, for phage-testing the strains of *Staph. aureus*; and the Medical Research Council technical laboratory staff for their assistance.

References at foot of next column

RADICAL SURGERY IN ADVANCED SQUAMOUS CARCINOMA

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THE treatment of advanced carcinoma requires courage and resource on the part of the surgeon; hence, any helpful experience merits documentation in the hope that it will encourage others to offer radical surgical treatment to patients otherwise doomed to lingering suffering with a fatal culmination. Since radiotherapy may be unsuitable for some of these patients, and in others it will have failed to eradicate the disease, there is no alternative treatment at present to surgery.

It is distressing that so many patients still present themselves for treatment in an advanced stage of cancer. This will be rectified with the development in this country of an educational programme for the public so that they can be informed of the warning symptoms of cancer and the facilities available for diagnosis and treatment. The establishment of diagnostic centres and treatment centres staffed by experts with special experience of cancer will be an important advance in its control.

Attention is called here to the value of radical surgical excision in certain types of advanced squamous carcinoma. The five patients whose case-records are cited were unsuitable for any other form of treatment than surgery, and it is emphasised that two of them had previously been pronounced untreatable and inoperable. After operation they returned to work and both have lived active lives for 7 years without recurrence.

CARCINOMA OF THE TONGUE

Case 1.—A man, aged 66, was seen on May 7, 1940, complaining of soreness of the tongue. On Sept. 27, 1939, a right partial glossectomy was performed at another hospital for a swelling of the tongue 5 cm. in diameter. This recurred later, and two weeks ago he was examined by another surgeon, who considered that any further treatment was impossible. The patient had syphilis at the age of 20.

On examination the tongue was scarred and severe leukoplakia was present. There was a large ulcer, with much induration of the right half of the tongue, spreading across the midline anteriorly. The right side of the floor of the mouth was also indurated. There were no enlarged lymph-nodes in the neck. Wassermann reaction negative.

Operations.—Ligation of the right lingual artery and excision of lymph-nodes in the right submaxillary region (May 14, 1940); and ligation of the left lingual artery and total glossectomy (May 29, 1940).

Histology.—The primary tumour of the tongue was a squamous carcinoma with much keratinisation. The lymph-nodes showed no carcinoma.

Result.—The patient was examined on Nov. 4, 1947, and no sign of carcinoma was present in the mouth or neck. He could talk and enunciate his words fairly well; swallowing was normal. The floor of the mouth appeared to contribute to these functions. Since the operation he had led an active life.

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CARCINOMA OF THE MAXILLA, NOSE, AND FACE

Case 2.—A man, aged 56, seen on Dec. 31, 1946, gave the following history. In 1932 a small ulcer appeared on the left side of his nose. In 1932–44 he received several treatments with radium and low-voltage X-irradiation elsewhere. In August, 1944, the ulcer was excised and the left antrum curetted, and this was followed in September, 1944, by a wider excision of the ulcerated area, including the antral mucosa and the left turbinate bones. During the subsequent two years diathermy excision and diathermy coagulation were performed on several occasions in an attempt to eradicate the disease.

On examination there was an extensive carcinoma of the left upper jaw, involving the soft tissues of the left side of the face and nose. A large hiatus was present at the nasofacial junction, opening into the left antrum. The carcinoma was spreading into the left orbit and nose and was starting to involve the upper right alveolus. The soft tissues of the nose and cheek were infiltrated.

Operation (Oct. 20, 1947).—A radical resection of the diseased area was performed after a preliminary ligation of the left external carotid artery. This excision involved the removal of the left upper jaw, the left eye, the floor of the orbit, the nasal septum, the greater part of the soft palate, a portion of the alveolus of the right maxilla, and the involved area of the soft tissues of the left side of the face. On Nov. 5, 1947, the outer part of the cavity was covered with a split-thickness skin graft.

Histology.—Mixed basal and squamous carcinoma.

Result.—In March, 1948, there was no evidence of recurrence; this was supported by microscopic examination of biopsies taken from various parts of the cavity. The patient's general health was excellent; he could eat and swallow his food well and could speak satisfactorily. A temporary prosthesis was being worn with good effect until reconstruction of the face could be carried out later. In January, 1949, areas of basal-cell carcinoma have recurred in the cavity.

CARCINOMA OF ALVEOLUS AND MANDIBLE

Case 3.—A man, aged 59, was seen on Feb. 3, 1948, with an ulcer in the left side of the mouth. Ten months earlier an ulcer appeared on the left lower jaw where his dentures fitted. This was treated elsewhere by three applications of radium.

On examination there was a carcinomatous ulcer involving the posterior third of the left lower alveolus, attached to the underlying bone and extending on to the floor of the mouth and the labio-alveolar sulcus. The left submaxillary lymph-nodes were enlarged. Radiological examination of the left mandible showed a round defect in the posterior part of the alveolar margin.

Operation (Feb. 18, 1948).—The horizontal ramus of the mandible, the carcinoma of the alveolus, and contiguous areas of the floor of the mouth and labio-alveolar sulcus were excised. The submaxillary and upper deep cervical lymph-nodes were excised with the tumour mass.

Histology.—Squamous carcinoma of alveolus; no involvement of lymph-nodes.

Result.—The wound healed well; good movement of the lower jaw was possible. No sign of recurrence on Dec. 21, 1948.

CARCINOMA OF THE EAR AND PETROUS BONE

Case 4.—A man, aged 53, was seen on Oct. 15, 1946, with ulceration of the right ear. In 1942 a small swelling appeared behind the right ear and had later involved the pinna. This was treated with irradiation at another hospital, but the ulceration increased and a right facial palsy developed recently.

On examination there was an extensive carcinomatous ulcer involving the right pinna and external auditory meatus, extending forward over the zygoma to the temporal fossa and backward to the mastoid process. The regional lymph-nodes were not enlarged.

Operation (Oct. 29, 1946).—Excision of the pinna with the diathermy knife. This was followed by a course of X-irradiation to the spreading anterior edge of the ulcer (45 kV., total dose, max. 6000 r, min. 5400 r in 14 days); and to the posterior and lower edge of the ulcer (45 kV., total dose, max. 5400 r, min. 4900 r in 14 days).

Further Operations.—March 26, 1947: radical excision of the carcinoma, including the ulceration of soft tissues, the right external auditory meatus, middle ear, a large part of the petrous portion of the temporal bone, and portions of the parietal and mastoid bones.

April 9, 1947: skin grafting (Thiersch's method) of cavity in skull.

May 14, 1947: skin grafting of small unhealed areas.

June 18, 1947: insertion of a fascial sling from the zygoma to the right angle of the mouth.

July 1, 1947 (by Mr. C. Dee Shapland): lateral tarsorrhaphy.

Histology.—Squamous carcinoma invading bone.

Result.—No sign of recurrence in February, 1948. Healing was satisfactory, and the patient had returned to work at a coalmine. In January, 1949, there was evidence of local recurrence of basal-cell carcinoma, but his general health was good.

CARCINOMA OF THE PENIS

Case 5.—A man, aged 48, was seen on Oct. 20, 1941, complaining of difficulty with micturition. For three years he had noticed increasing dysuria, accompanied later by hæmaturia, suprapubic pain, and a constant ache in the perineum. Recently the dysuria had become severe, and on admission he had complete retention of urine. He had been examined by another surgeon and a radiotherapist, who had both pronounced the condition inoperable by surgery and untreatable by irradiation.

On examination his general condition was good. The urinary bladder was distended as high as a point midway between the umbilicus and the ensiform cartilage. The penis had been destroyed by a carcinoma except for the stump, 1/4 in. long, where a firm collar of growth was present. The regional lymph-nodes in the groin were not enlarged.

Treatment.—The urinary bladder was emptied by suprapubic puncture, 66 oz. of urine being evacuated.

Operation (Oct. 27, 1941).—Total amputation of the penis. The corpora cavernosa were separated from the pubic bone, the proximal end of the urethra was implanted in the perineum, and the testicles, with the greater part of the scrotum, were excised.

Histology.—Squamous carcinoma of the penis.

Progress.—Teleradium therapy was given to the regional lymph-nodes in both groins (dose 4200 r in 85 hours). The patient was discharged on Jan. 1, 1942. The wound had healed by primary union and micturition was normal.

Result.—No sign of carcinoma present in November, 1948. The patient had been at work since discharge from hospital. Micturition was normal.

DISCUSSION

These patients with advanced squamous carcinoma in different parts of the body demonstrate the advisability of carrying out radical surgical excision with the possibility of a good measure of success. They were suffering considerable pain and disability, apart from the fatal prospect. As a result of operation the pain was completely relieved and the disability corrected, so that they could lead normal lives and do useful work, in two cases for 7 years; the other patients were operated on more recently, and 2 have recurrent basal-cell carcinoma.

If success is to be achieved, the excision must be radical so that the whole of the diseased area is removed widely, irrespective of the deformity which is produced. These patients are often in poor general health; hence full preoperative treatment must be given, and supportive treatment may also be required during the operation. In the postoperative period the usual measures for the maintenance of the patient's nutrition and the control of infection are instituted. There are certain other additional problems to be elucidated.

Treatment of Regional Lymph-nodes.—Block dissection rather than irradiation is preferable, provided the lymph-nodes are removable. In all forms of squamous carcinoma, when enlarged mobile lymph-nodes are present, block dissection should be done, unless there is a definite contra-indication to the operation. If the lymph-nodes are not enlarged clinically, the site of the primary disease is taken into account in deciding whether or not to do block dissection. In carcinoma of the tongue block dissection is recom-

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mended because experience has taught that lymph-node metastases may be present without causing clinical enlargement. The same applies to carcinoma of the alveolus, floor of the mouth, fauces, and tonsil; when the lip is involved the patient is kept under observation and block dissection is done if the nodes become enlarged.

This opinion was confirmed recently in the case of a woman, aged 75, with an early carcinoma on the lateral border of the anterior half of the tongue and no enlarged cervical lymph-nodes on palpation. The carcinoma was excised, and because of the patient's age, early stage of the primary disease, and absence of palpable lymph-nodes it was decided to keep her under periodic review. Nine months later an enlarged upper deep cervical lymph-node was found, and a radical block dissection was therefore done; microscopy showed squamous-cell carcinoma in one lymph-node.

In the cases of carcinoma of the upper jaw and petrous bone it was decided not to do a block dissection in the absence of enlarged lymph-nodes, though the primary disease was very extensive. It appears justifiable to keep such patients under observation and to remove the lymph-nodes if they become enlarged.

As regards inguinal lymph-nodes, since block dissection may be followed by lymphatic obstruction and œdema of the lower limb, it is justifiable to keep these patients under observation and to excise the lymph-nodes if they enlarge.

Postoperative Irradiation.—In these cases of advanced squamous carcinoma a full course of irradiation with high-voltage X rays, teleradium, or other forms may have been given with failure to eradicate the disease; hence additional treatment after operation may be contra-indicated. Further, the object of the operation must be the radical extirpation of the disease; hence, it is assumed that all malignant tissue has been removed. This assumption is tested by subsequent review; if there is a recurrence, irradiation is considered, together with other methods of treatment, including the destruction of the local diseased area by diathermy.

Repair of Defects.—After such extensive operations repair of the defects is an important part of the treatment, especially in the face, jaws, and skull. Skin grafting plays an important part, and I advise delayed skin grafting after 12 months to exclude early recurrence of the cancer; microscopy of the excised tissues will give some indication about this possibility. We have found split-thickness skin grafts of value to line cavities such as those produced in the petrous bone; the pedicle skin graft is used for the repair of facial defects. Patients with severe defects of the face are given a temporary prosthesis to wear during the interval before reconstruction work can begin. (I have had the opinion of the late Mr. P. P. Cole in plastic surgery, and have been greatly helped by his advice in carrying out these reconstruction operations.)

Team-work.—A surgeon responsible for these radical operations for cancer should have knowledge of reconstructive surgery and be familiar with the possibilities for each patient. The help of specialists in plastic surgery, eye, ear, and radiotherapy, should be sought, and full coöperation established both in the planning and performance of the operation and subsequent reconstruction. It might be an advantage to establish these teams in centres where such extensive operations for cancer are performed.

SUMMARY

Attention is called to the value of radical surgical excision in certain cases of advanced squamous carcinoma.

Five examples are described—carcinoma of the tongue; of the maxilla, nose, and face; of the alveolus and mandible; of the ear and petrous bone; and of the penis.

The cases of carcinoma of the tongue and of the penis were pronounced hopeless; the two patients have lived busy and useful lives for 7 years without recurrence.

The patient operated on for carcinoma of the ear and petrous bone was also returned to work and was free from recurrence 11 months after operation; 22 months after operation there is local recurrence, but his general health is good.

The treatment of lymph-nodes, postoperative irradiation, and the repair of defects are described.

The importance of team-work in the management of these advanced cases of carcinoma is emphasised.

INFLUENCE OF PREVIOUS DIET ON THE EFFECT OF GLUCOSE IN PERIODIC PARALYSIS

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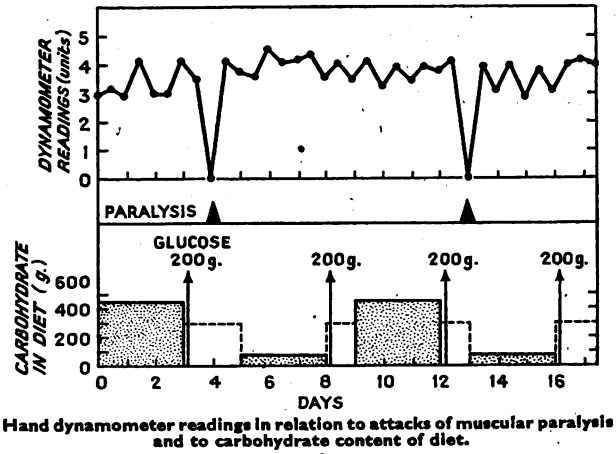
Shinosaki (1925–26) showed that attacks of periodic paralysis could be precipitated, in patients subject to them, by the ingestion of large amounts of carbohydrate. Fat or protein had no such effect. Since the publication of investigations by Aitken et al. (1937) and Allott and McArdle (1938) interest has centred on the rôle of potassium in this disease (Pudenz et al. 1938, Ferrebee et al. 1940, Danowski et al. 1948). It is now known that during paralysis there is hypopotassæmia, renal retention of potassium, and migration of potassium from the extracellular to the intracellular space; but the exact relation between these findings and the fact that an attack can be precipitated by the ingestion of carbohydrate is not clear. It has been thought that the development of paralysis and the changes in potassium metabolism are in some way related to the cycle of carbohydrate combustion in skeletal muscle. If this is so, it might be expected that the effect of glucose would to some degree depend on the previous carbohydrate intake. Since the demonstration of "starvation diabetes" by Claude Bernard (1859) numerous investigations have shown that after a period of carbohydrate starvation certain abnormalities of carbohydrate metabolism occur which seem to reflect a decreased peripheral utilisation of glucose (Chambers 1938, Samuels 1947, Lundbaek 1948). I have found recently that the glucose uptake of rat diaphragm in vitro is considerably decreased when the rats have been kept on a carbohydrate-free diet (Lundbaek and Stevenson 1948). It was therefore decided to try the effect of glucose after high-carbohydrate and low-carbohydrate diets in a patient with periodic paralysis.

Aged 21, he had had typical attacks of periodic paralysis since the age of 19. An uncle, a grandfather, and a great-



Hand dynamometer readings in relation to attacks of muscular paralysis and to carbohydrate content of diet.

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grandfather had also had periodic paralysis. Physical examination between attacks was completely negative. During attacks areflexia and loss of electrical irritability of the paralysed muscles were found.

The patient was given two diets successively for a period of three days, one with a carbohydrate content of about 450 g., the other containing about 70 g. of carbohydrate. On the morning of the fourth day 200 g. of glucose was given by mouth, and the patient was allowed to eat the regular hospital diet for the rest of the day. Muscle strength was estimated with an ordinary hand dynamometer. The result of the experiment is shown in the accompanying figure.

It is seen that glucose given after a period of high-carbohydrate diet precipitates a typical attack of paralysis. After low-carbohydrate diet no such attack is precipitated. Since it is known that the glucose uptake of muscle cells is reduced after carbohydrate starvation, the absence of a paralysing effect of glucose after low-carbohydrate diet in this experiment seems to indicate that the development of paralysis is directly related to the peripheral transfer of glucose from tissue fluid to cells.

SUMMARY

After periods of high-carbohydrate diet ingestion of 200 g. of glucose precipitated typical attacks in a patient with periodic paralysis. After periods of low-carbohydrate diet no such effect was seen.

The development of paralysis seems to be directly related to the migration of glucose from the extracellular space to the cells of skeletal muscle.

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CEREBRAL ABSCESS IN AN INFANT

FOLLOWED BY RECOVERY

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THE prognosis of cerebral abscess in infancy is always extremely serious but the present case proves that the abscess may resolve. It also illustrates once more the amazing resilience of the newborn.

Sanford (1928) reported 2 cases of brain abscess in infants under one year of age and reviewed 17 published cases. Others have since been reported by Lesné et al. (1932), Pelfort et al. (1941), and Baumoel et al. (1942). Though some of the infants were treated with sulphonamides none received penicillin and all died. Commonest at the age of three months, these abscesses have usually been associated with previous sepsis elsewhere, most often either in the ear or on the surface of the body. The commonest infecting organism has been the staphylococcus; streptococci, pneumococci, and even *Bacterium coli* have also been encountered. In the present case a staphylococcal infection of the left frontal lobe arose during a fairly severe inflammation of the face and of the left nasal cavity.

CASE-REPORT

A boy, aged three months, was transferred as a case of suspected cerebral abscess from the Bolton Royal Infirmary on April 18, 1946, to St. Mary's Hospital for Women and Children, Manchester, where he was placed under the care of the neurosurgical service of the Manchester Royal Infirmary.

History of Illness.—Born on Jan. 14, 1946, at full term, the third child of healthy parents, he then weighed 7 lb. 7 oz. No instruments were used during delivery, which was apparently without incident apart from a small perineal tear. He was breast-fed. Two brothers were alive and well, though one had been operated on for hypertrophic pyloric stenosis. On Jan. 18 he had a slight discharge from the left eye and the left nostril and also a few spots on both cheeks. On Jan. 25 a large spot with a yellow centre on the right cheek was squeezed. By Feb. 18 there was a purulent discharge from the left upper gum and left nostril; the eyelids and conjunctiva of the left eye were swollen and dusky red, and the eye was slightly proptosed. Treatment for a week with sulphonamide led to improvement, but the proptosis remained.

On Feb. 27 he was admitted to Bolton Royal Infirmary. Temperature 100°F. White cells 11,800 per c.mm. (polymorphs 49%, lymphocytes 34%). Radiography: no obvious infection of the antrum. Penicillin and sulphadiazine caused resolution, and the proptosis disappeared. After discharge from hospital on March 13 he was well for three weeks, but on April 2 had a convulsion which consisted in a coarse tremor of a few minutes' duration, beginning in the right side of the face and spreading first to the right arm and then to the left arm. He vomited profusely. Readmitted to Bolton Infirmary, he was found to have neck rigidity with Kernig's sign positive; the fontanelle was tense and bulging. Temperature normal. White cells 22,600 per c.mm. (polymorphs 45%, lymphocytes 50%); Wassermann reaction negative in both blood and cerebrospinal fluid (C.S.F.). Radiography of skull negative. A nasal swab from the left side gave *Staph. hæmolyticus* in pure culture. C.S.F.: under increased pressure; cells 150 per c.mm. (polymorphs and lymphocytes); protein 50 mg. per 100 ml.; chlorides 700 mg.; culture sterile.

In spite of penicillin and sulphadiazine his general condition did not improve, but there were no more convulsions.

Examination and Investigations (April 18).—An infant with moderate cranial enlargement; pale, not dehydrated; irritable, but crying lustily at times. Anterior fontanelle very large and moderately tense. Ears and fauces normal; lungs clear. No obvious neck rigidity; Kernig's sign negative. No cranial nerve defect; good power in all limbs, with equal tone and deep reflexes; no areas of anæsthesia; plantar reflexes extensor. Blood: red cells 4,220,000 per c.mm.; Hb 66%; white cells 13,800 per c.mm. (polymorphs 42%, lymphocytes 30%). C.S.F.: clear, pressure 400 mm. (no block); 400 cells per c.mm. (polymorphs and lymphocytes); protein 120 mg. per 100 ml.; chlorides 620 mg.; Pandy test positive; no organisms seen in film; culture sterile. Radiography of chest and of skull negative, apart from obvious enlargement of skull.

Diagnosis.—The differential diagnosis lay between cerebral abscess and chronic adhesive meningitis associated with hydrocephalus. The baby was too well to be harbouring a subdural empyema, and a non-infective lesion, such as a subdural hæmatoma or a new growth, would not have accounted for so many cells in the C.S.F. As the head was becoming larger each day it was decided to perform a diagnostic needling of the brain and meninges via the fontanelle. Any fluid collection found could then be aspirated; ventriculography could also be undertaken if necessary.

Operation (April 24).—Under local anæsthesia with procaine, the scalp was punctured on each side of the midline over the most lateral part of the anterior fontanelle. Brain cannulæ were passed on each side downwards and a little laterally. No fluid was found below the meninges. Clear C.S.F. spurted from the right lateral ventricle after removal of the stylet: it was immediately replaced. The cannula on the left side entered an abscess cavity about 1 cm. below the dura mater, and thick green pus gushed out. The abscess was gently aspirated with a syringe until no more pus welled up, and 3 ml. (30,000 units) of penicillin and 2 ml. of 'Thorotrast' were injected into the cavity. The cannula was then removed.

The laxity of the cranial vault following the reduction in size of the whole head was remarkable. The head was rather like an old partially deflated balloon, and one wondered whether the baby could survive the operation. Though he was very shocked, and remained so an hour or two, he managed to take and retain his feed six hours after operation.

Pus Obtained.—Amount, 145 ml. Smear showed many gram-positive cocci. Culture yielded penicillin-sensitive *Staph. pyogenes.*

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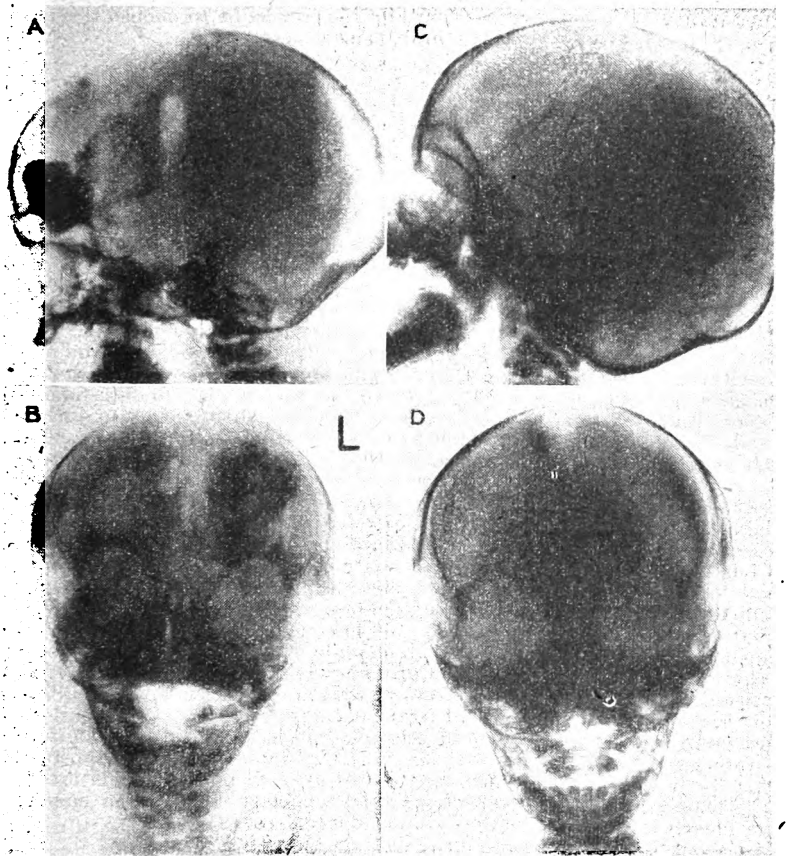

Radiograms after thorotrast: A, lateral, and B, anteroposterior views showing air and thorotrast in abscess cavity after first aspiration (April 24, 1946); C, lateral, and D, anteroposterior views showing residual cavity (Oct. 28, 1946).

Radiography after Thorotrast.—A lateral film showed an enormous abscess cavity in the left frontal region, extending posteriorly, at its highest point, to the level of the posterior margin of the shadow of the pinna—i.e., ending adjacent to, if not invading, the motor cortex. Superiorly, inferiorly, and anteriorly it reached within a few millimetres of the corresponding limits of the frontal lobe. An anteroposterior film showed that the abscess extended almost from the lateral surface of the cerebral hemisphere to within 1 cm. of the medial surface. In short, almost the whole of the left frontal lobe was replaced by abscess cavity (see figure).

Progress in Hospital.—Though shocked by the first two aspirations and lying quietly for two or three days the baby continued to take its breast-feeds. Systemic penicillin was given intramuscularly, and the abscess was aspirated as often as the condition demanded. On April 25, 25 ml. of pus was removed by needling the cavity through the fontanelle, and penicillin 15,000 units was inserted. (Staphylococci were grown from the pus.) On April 28, 3 ml. of fluid was taken off, and penicillin 15,000 units was inserted: no shock. On April 30, 2 ml. was removed and 15,000 units of penicillin inserted.

On May 7, 2 ml. of C.S.F. was obtained; it was sterile but contained 14 cells per c.mm.; and protein 30 mg. per 100 ml. At the sixth and final aspiration, on May 14, only a trace of fluid was obtained; 2 ml. of thorotrast was inserted, and radiography showed that the abscess cavity had almost collapsed. White-cell count: 9000 per c.mm.

On June 6 the baby was alert, with fontanelle sunken, and minimal neck rigidity. Left VI nerve paresis. Limbs normal, optic discs, from a brief glimpse, apparently normal. He was discharged home. He had received 15,000 units of intramuscular penicillin 3-hourly for 18 days besides that injected directly into the abscess. In hospital his temperature was hardly ever raised and there were no convulsions. Feeding, which was from the breast, was remarkably normal.

Progress at Home.—The mother, writing three months after the child's discharge, said he was in good health and developing normally. She had noticed that occasionally the right pupil appeared to be larger than the left, and that there had been some stiffness of the right arm, together with an infolding of the right thumb into the palm; but these signs had disappeared. Examined in the outpatient clinic on Oct. 28 he had no abnormal neurological signs. Radiography of the skull revealed the thorotrast and showed that the abscess cavity had completely collapsed (see figure).

A complication arose in December, 1946. During two months he had a series of minor convulsions, described by his mother as follows: "Suddenly his head ducks as though he is cringing from a blow, and simultaneously there is a twitch of all four limbs or sometimes of the right arm alone. This occurs four or five times with counts of perhaps ten in between. It is as though someone has momentarily loosened one of a marionette's strings and then tightened it again." These attacks usually took place during feeding, and there would be three or four in a day, though on some days there were none. They ceased spontaneously, the last occurring on Feb. 2, 1947.

About this time the baby also had a short-lived discharge of pus from the left upper gum near the first incisor tooth and some swelling of the upper lip. He was admitted to hospital for ten days, but no maxillary or dental disease was detected on radiography, and the discharge, which ceased after two days, has not recurred.

Follow-up.—Seen at home on April 25, 1947, exactly a year after the first aspiration, the baby appeared to be perfectly normal both mentally and bodily and like any other baby of fifteen months. His mother said he was generally alert, and that he was as normally developed as his two brothers had been at the same age. He was walking well and he laughed and played with great energy, picking up objects equally well with either hand. Certainly there seemed to be no gross weakness of arm or leg. Height 30 in. Weight 21 lb. 14½ oz. Cranium of normal size in relation to body. Fontanelle still open, but depressed. No asymmetry of the face. No proptosis. Eight teeth present; some discoloration of the first upper incisor tooth, but it was not deformed or loose. No discharge and no obvious sinus.

Neurological examination proved negative, except for equivocal plantar responses, similar in the two feet, and an indefinite suggestion of flaccidity of the right leg. When the parents were last heard from, at the end of June, 1948, the child was healthy, talking, and showed no obvious disability.

COMMENTS

The abscess in this case probably arose from infection of the left cheek and thrombophlebitis of the facial veins, the infection travelling up these veins to the cranium. The left proptosis and orbital œdema suggest cavernous-sinus thrombosis. Birth trauma does not seem to have been a factor. There is now no clinical or radiographic evidence of maxillary infection, but because of the recent gingival discharge one has to bear this condition in mind.

Systemic penicillin undoubtedly played a great part in localising the infection, and by local injection it sterilised the abscess.

Whereas in adults the skull is a rigid box, in infants it is more lax and can distend to accommodate a space-occupying lesion. Because of this it seems that the earliest sign of an intracranial abscess may be enlargement of the head, and the effects of pressure, such as vomiting and coma, may appear late. The head can also contract again, as this case shows. Indeed it seems that the collapse of the abscess cavity was greatly facilitated by the falling-in of the parietes.

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As regards prognosis, the minor convulsions arising during a bout of indifferent health suggest the possibility of epilepsy in later life.

As cerebral abscess in infancy may be associated with few physical signs, there should be no delay in using diagnostic measures, such as needle puncture and ventriculography, in any doubtful case.

I am indebted to Prof. Geoffrey Jefferson, F.R.S., head of the neurosurgical unit, for his permission to publish this case and for his advice in its management.

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Reviews of Books

An Atlas of Bone-Marrow Pathology

M. C. G. ISRAËLS, M.SC., M.D., M.R.C.P., lecturer and deputy director, department of hæmatology, University and Royal Infirmary, Manchester. London: Heinemann Medical Books. 1948. Pp. 79. 30*s*.

THIS book sets out to provide an authoritative, accurately illustrated, account of the bone-marrow in health and disease, for the guidance of physicians and pathologists. It contains 12 coloured plates made from drawings by Miss D. Davison, medical artist to the University of Manchester, and 48 pages of text.

The chapter on nomenclature and development of the blood-cells is happily short and dogmatic, the author making use of the nomenclature which is now commonly employed in this country and which he himself has done so much to stabilise. The chapter on technique is somewhat superficial; there is no note either of difficulties, or, for example, of the significance of failure to obtain a reasonable sample when aspiration is performed by a competent and practised operator. Indeed, in the whole volume there is no mention of the fibrotic conditions of the marrow in which aspiration may be difficult and in which the value of the section, obtained by trephine, is undoubted. A chapter dealing with the morphology of the marrow cells is commendably definite. It is, however, a great pity that the coloured plates, to which reference is given, do not contain at least one clearly marked cell which Dr. Israëls would regard as illustrating, beyond argument, each of the types which he is so careful to define in words. The most valuable chapter in the book, and one that will appeal especially to physicians, deals with differential diagnosis and indications for sternal puncture. The author rightly says that few physicians or pathologists carry the normal figures around with them, and he recommends a qualitative rather than a quantitative assessment of a marrow smear, under a number of headings from which general conclusions can be drawn. Excellent examples of this method of assessment are given, covering most of the blood conditions in which marrow examination is useful.

The plates have been well executed and beautifully reproduced, though Miss Davison's extremely attractive but rather pastel style tends to make a pleasing picture rather than bring into prominence important features. For example the nucleoli of the myeloblasts and lymphoblasts in plates 4, 6, and 11 are, in many cases, so vague as to suggest either poor staining or a lack of proper illumination and optimum focus. The effect is artistic but not informative. Magnifications should have been stated on those plates that illustrate individual cells divorced from a background of red cells.

Taken as a whole, and discounting minor criticisms, this book is very well produced and is a most valuable addition to hæmatological literature, with an appeal to both physician and pathologist.

Barbarism and Sexual Freedom

ALEX COMFORT, M.B., D.C.H. London: Freedom Press. 1948. Pp. 68. 3*s*. 6*d*.

Dr. Comfort's premises in this little book will hardly be questioned. He thinks that young people, growing up in a society where wars are likely and conscription a necessity, have little opportunity for normal sexual maturation, and indeed are seriously hindered in reaching the normal expression of mature sex—the responsible rearing of a family. Marriage, he holds, begins with the birth of a child; and parents who have children should be permanent sexual partners. "The essential points are the voluntary character and the maturity of the parties, the permanence of the relationship and the definite intention of forming a family community . . . there is no word other than marriage which can be used intelligently for this relationship. . . ." He finds marriage in our society but a travesty of it. The parties are often immature and irresponsible, and neither their unstable personal inclinations nor their duty to their children serves to make their partnership enduring. His book is largely concerned with the remedies, as he sees them. He surveys what we know of human sexual practices, classing them all as current manifestations of sex, and not seeking to force them into a moral or legal classification as either normal or abnormal. Most people will appreciate this just and realistic approach to a subject much obscured by prejudice and unconscious emotion. His plea for reform in the punishment of sexual offences will also be valued, for in this respect the penal code is undoubtedly badly out of date. Some of his other remedies are much less acceptable; few, for instance, would endorse his suggestion that young people should be deliberately instructed in sexual equivalents during adolescence, however firmly they may believe that anxiety about such equivalents should be allayed. Dr. Comfort writes as an anarchist, from which it surely follows that he must be both idealistic and intolerant of irrational compromise. Yet he knows the mind of man so well that it is astonishing that he does not know it better. His book is intensely interesting; but ultimately he escapes from real issues into a utopian prospect where everybody behaves as society and Dr. Comfort would like him to do.

Modern Psychiatric Practice (2nd ed. London: J. & A. Churchill. 1948. Pp. 275. 12*s*. 6*d*.).—The second edition of Dr. W. Lindesay Neustatter's refreshingly honest and unpretentious handbook contains two new chapters, on psychopathy and on neuropsychiatry, as well as changes in the sections on treatment, hysteria, and the psychoses. The section on disorders of children remains substantially as before, and, in its robust avoidance of the jargon and guesswork so prevalent in writings on this subject, is one of the best features of the book.

Annual Review of Microbiology (Vol. II. Annual Reviews, Stanford, California. 1948. Pp. 532. 36*s*.).—Mr. Charles E. Clifton, Mr. Sidney Raffel, and Mr. H. Albert Barker edit a series of critical essays by contributors working in various fields of microbiology. This new volume treats at length various important branches of the subject, and should thus free future contributors to consider details of current work. Topics covered here include bacterial metabolism, growth factors for micro-organisms, antibiotics, and the mode of action of chemotherapeutic agents.

Fundamental Principles of Bacteriology (3rd ed.), and **Laboratory Manual on Fundamental Principles of Bacteriology** (3rd ed.) (London: McGraw Hill. 1948. Pp. 730 and 176. 36*s*. and 13*s*. 6*d*.).—Beyond the backyard of medical bacteriology is the field of fundamental information about micro-organisms which Prof. A. J. Salle attempts to cover in the first of these books. Profusely illustrated with chemical formulæ, it explains bacterial activities in simple terms and warns against uncritical acceptance of both old and new theories. It has been expanded and completely rewritten, and there are valuable chapters on the bacteriology of food, air, and soil, and also descriptions of the growth factors required by bacteria and of bacterial and virus diseases of plants. Study of organisms in overcrowded and mixed communities has already led to the discovery of antibiotics, and it is encouraging to find a chapter devoted to the associations of bacteria. There are good illustrations and a liberal bibliography, and for those who wish to put theory to test the companion laboratory manual tells how this may be done.

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THE LANCET

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Gastric Vascular Shunts

IN our anxiety to treat disease we often forget that the study of the normal must be the rational basis of any understanding of the abnormal. The work of BARCLAY and BENTLEY [1] on the effect of trauma on the gastric blood-vessels is a salutary lesson on the worth and implications of intimate anatomical studies of the normal. They bring forward evidence for the existence of a system of arteriovenous anastomoses in the submucosa of the stomach wall. These shunts, as they are now termed, are probably under sympathetic control; their opening by nervous stress or trauma will deprive the mucosa of its vital blood-stream. This observation may well provide a new concept of the ætiology and rationale of management of peptic ulceration. When TRUETA and his colleagues at Oxford [2] demonstrated their renal shunt mechanism, many predicted similar gastric shunts but none could definitely say "it is so." Without BARCLAY'S brilliant technical achievement [3] in developing micro-arteriography in 1945–47 the first step in such a discovery would not have been possible. But, as FRANKLIN [4] rightly comments, in retrospect it seems clear that it was the rush to apply the discovery of X rays to the pathological that shunted attention from the importance of normal patterns.

To demonstrate the gastric vessels, BARCLAY and BENTLEY injected radiopaque material at a pressure of 150 mm. Hg into the arteries of the stomach excised at operation or necropsy and then took arteriograms of the stomach wall; transverse sections of different areas of stomach were then cut and subjected to micro-arteriography. To prevent overlapping of the vascular patterns, two different radiopaque materials were used—one of larger particle size, for the larger arteries down to the arterioles, and a thinner colloid preparation for the finer ultimate branches. A remarkable fact was observed—the finer mucosal vessels could be displayed over large areas in the cadaver stomach, but they hardly filled at all in 12 stomach specimens excised for duodenal ulcer. To these trained minds this observation suggested either that the fine mucosal vessels were in a state of agonal spasm, or that the operative trauma had opened an easier pathway for the flow of injected material. They chose the latter concept; renal shunts were known to open with trauma and very likely this applied to the stomach. Their next experiment was to take a sample of blood from a surface vein of the stomach immediately on abdominal section, and another a few minutes later; the oxygen saturation rose from 74 to 91%, suggesting that trauma had opened up arteriovenous communications. To exclude the reflex effects of such trauma seemed the necessary next step. A patient undergoing gastrectomy was given high spinal anæsthesia, to level T1–2; in this excised stomach, as distinct from all other operative specimens, the pattern of the mucosal vessels was clearly and abundantly defined by injection. The evidence was taken to indicate that the opening of the gastric shunts by operative trauma had been prevented by the spinal anæsthetic.

The word "shunt" is a little confusing. Apparently there are no arteriovenous anastomoses of the commonly accepted kind—that is, there are no nerve-controlled sluice-gates, no glomus with muscular walls to hold and release the blood, and even propel it on, as we find in limb shunts. In the stomach, as in the kidney, the mechanism seems to be one of redistribution, a shunting into potential alternative routes. The submucosa is like a vast Clapham Junction, in which blood may be diverted to distal major towns, even to the neglect and suffering of local suburbia. The report of BARCLAY and BENTLEY is a preliminary one, and there are still a few gaps difficult to leap across. Mere opening of the shunts does not seem an adequate explanation for the non-filling of the mucosal vessels; at a pressure of 150 mm. Hg the by-paths would have to be relatively very large to prevent the fluid flowing at all into the tributaries. As in the cortex of the kidney, it is reasonable to argue that these mucosal vessels are probably also "peculiarly reactive" to trauma, and operative handling may induce in them an intense vasoconstriction. The fact that the fine vessels can be injected in the cadaver would be in accord with this view. Such vascular spasm, too, is known to be recalcitrant and often will not relax in response to sympathetic block or denervation—to which the multiple gastric vessel ligatures in gastrectomy must correspond. Arterial spasm elsewhere can be maintained for several days, even when the vessel contains no circulating blood. The full filling of the mucosal vessels after spinal anæsthesia suggests that there is an added factor of complete vasomotor paresis of the fine vessels; caught in their new tone posture by the partial gastrectomy, they fill even better than the relaxed cadaver vessels.

From the physiologist's point of view, the identification of gastric shunts adds further detail to the concept of a particular hæmodynamic mechanism. As FRANKLIN [4] points out, the body's total blood volume is not enough to fill the entire circulatory system at once; such a mechanism converts each organ into a ready blood-donor, willing to lend to, and sometimes even to suffer for, its fellow. For the kidney, CORT, working in FULTON'S laboratory at Harvard, has shown that the master switch for

1. Barclay, A. E., Bentley, F. H. *Brit. J. Radiol.* 1949, **22**, 62.
2. Trueta, J., Barclay, A. E., Daniel, P. M., Franklin, K. J., Prichard, M. M. L. Studies of the Renal Circulation. Oxford, 1947.
3. Barclay, A. E. *Brit. J. Radiol.* 1947, **20**, 394.
4. Franklin, K. J. *Science News.* **10**. London: Penguin Books, 1949.

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shunting lies in area 13 of the cerebrum—i.e., in the supraorbital plate area of the frontal lobe, an area known to be connected with other visceral function.

BARCLAY and BENTLEY have refrained from commenting on the clinical applications of their findings. ALVAREZ,[5] in his editorial on their work, has no such qualms about hypotheses, for he knows that without the preliminary hypothesis America would never have been discovered. Indeed, as TROTTER observed, the only danger of a hypothesis is a too passionate attachment to it. ALVAREZ points out that these findings provide a reason for the acute peptic ulceration associated with certain brain tumours and thyrotoxic cases. The localised character of the peptic ulcer, when the ischæmia arising from shunt action is widespread, he finds difficult to explain; it is worth noting from the work on renal shunts that the blood does not necessarily pass exclusively through any one route but may do so in varying proportions. There is clearly a wide field for further inquiry. It does not require much imagination to appreciate the urgent need to apply the technique of micro-arteriography to the study of other organs.

Further Trials of Aureomycin

AUREOMYCIN,[6] or 'Duomycin' as it is called commercially in America, has the widest range of activity of any known antibacterial substance. It is also well absorbed by mouth and seems to be relatively free from side-actions. It is not yet generally obtainable in England, but small quantities have been sent from the U.S.A. for testing, and manufacture is being rapidly developed over there.

Though it has proved as effective as penicillin or the sulphonamides in pneumococcal and meningococcal infections in man,[7] it is in the treatment of infections with gram-negative bacteria, viruses, and rickettsias that aureomycin is likely to be most useful. Brucellosis, one of the gram-negative coccal infections that until recently had resisted specific treatment, has shown some response to a combination of streptomycin and sulphadiazine,[8] but the dosage of streptomycin required caused vestibular dysfunction and other toxic effects in many of the patients. Weight for weight, streptomycin is more active in vitro than aureomycin against several species of brucella, but in view of the lower toxicity of aureomycin SPINK and his colleagues[9] treated 24 Mexicans suffering from *Br. melitensis* infection—the more virulent form of brucellosis—with aureomycin and sulphadiazine by mouth. The clinical results far surpassed the expectations of the investigators, who had already had considerable experience with streptomycin and sulphadiazine in brucellosis. During the trial it became evident that aureomycin alone, in relatively small doses by mouth, dramatically altered the course of the disease; the results obtained were just as good when the sulphadiazine was omitted. Every patient was febrile before treatment began and became afebrile within three days of starting aureomycin. All showed clinical improvement and had a sterile blood-culture, though 3 subsequently relapsed. One critically ill patient who was pregnant did not abort. SPINK and his colleagues had previously observed the clinical course of undulant fever in hundreds of patients receiving vaccines, sulphonamides, and streptomycin, and no other form of therapy had produced such striking clinical and bacteriological improvement as aureomycin. The side-effects observed were mild and in no way comparable with those of streptomycin. Most of the patients had none, but a few complained of nausea or diarrhœa, and some had an abrupt rise of temperature, tachycardia, and a fall in blood-pressure. These apparently were due to too large an initial dose of drug, since a reduction in dosage lessened these side-effects. Whether the drug will prove equally effective in *Br. abortus* infections remains to be seen. And for the complete evaluation of any remedy in brucellosis a long follow-up period is essential. On the available evidence, however, aureomycin is the best agent tried so far.

According to reports from the Mayo Clinic,[10] aureomycin is active against spirochætes. Experimentally it has proved to be more effective (weight for weight) than penicillin in the treatment of relapsing fever in mice and leptospirosis in hamsters. In 2 patients given aureomycin by mouth for sixteen days primary syphilitic lesions were completely healed, though the serological tests for syphilis were still positive. One drawback to the administration of the drug over long periods is that it inhibits the growth of the intestinal organisms which synthesise B vitamins; so unless vitamin supplements are given the patient may develop signs of vitamin-B deficiency, such as glossitis and angular stomatitis. This is also true of penicillin and the sulphonamides.

Following the observation that aureomycin can protect mice and guineapigs infected with the rickettsias of Q fever, Rocky Mountain spotted fever, murine typhus, and rickettsial pox,[11] it has been tried clinically in Q fever and Rocky Mountain spotted fever. In California LENNETTE and his colleagues[12] gave aureomycin to 23 patients with Q fever, using 90 untreated patients as controls. Symptomatic improvement was noted in all but one of the treated group, and the duration of fever was considerably less than in the control group. Two treated patients relapsed but became afebrile after a second course of the drug. A group of workers at Washington and Baltimore[13] who have been investigating Rocky Mountain spotted fever since its identification on the east coast of the U.S.A. in 1931 have noted the effect of aureomycin on 13 cases and describe the response as very impressive. A rapid fall in temperature was paralleled by a striking clinical improvement within 24–48 hours of starting treatment. The results with aureomycin are said to be superior to those with *p*-aminobenzoic acid, which also has a specific action in rickettsial infections but causes leucopenia and hepatic damage in some patients. Apart from nausea and vomiting no toxic effects were observed in the patients receiving aureomycin.

5. Alvarez, W. C. Editorial. *Brit. J. Radiol.* 1949, **22**, 61.
6. See annotations, *Lancet*, 1948, ii, 618; Jan. 8, p. 69.
7. Collins, H. S., Paine, T. F., Finland, M. *Proc. Soc. exp. Biol., N.Y.* 1948, **69**, 263.
8. Spink, W. W., Hall, W. H., Shaffer, J. M., Braude, A. I. *J. Amer. med. Ass.* 1948, **136**, 382.
9. Spink, W. W., Braude, A. I., Castaneda, M. R., Goytia, R. S. *Ibid*, **138**, 1145.
10. Heilman, F. R. *Proc. Mayo Clin.* 1948, **23**, 569. O'Leary, P. A., Kierland, R. R., Herrell, W. E. *Ibid*, p. 574.
11. Wong, S. C., Cox, H. R. *Ann. N.Y. Acad. Sci.* 1948, **51**, 290.
12. Lennette, E. H., Meiklejohn, G., Thelen, H. M. *Ibid*, p. 331.
13. Ross, S., Schoonbach, E. B., Burke, F. G., Bryer, M. S., Rice, E. C., Washington, J. A. *J. Amer. med. Ass.* 1948, **138**, 1213.

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National Formulary 1949

THE new *National Formulary* (1949) replacing the *National War Formulary* is produced by the Joint Formulary Committee, appointed mainly by the B.M.A. and the Pharmaceutical Society, but including representatives of the Ministry of Health, the Services, and the Royal College of Physicians. Medical members form two-thirds of the new committee, compared with less than half of the committee for the *N.W.F.*

There is rarely any therapeutic advantage in the multiplication of prescriptions differing only in minor details; and this publication aims at standardising and simplifying these formulæ. For titles Latin names are still used, and the official abbreviations given are useful for reference. Brief notes are included on the pharmacology and therapeutics of barbiturates, sulphonamides, some hormones, and liver extracts. The special requirements in prescriptions for schedule-4 and D.D.A. drugs are tabulated, and rules are given for "repetitions" allowed in the case of private prescriptions. The appendix contains a long list of proprietary names with exact or analogous official equivalents. There are also tables for identification colours for medical gas cylinders. A comprehensive index includes older names of certain preparations.

The preparations of general medical interest are mainly in the sections on tablets, injections, and mixtures. Nearly 90 TABLETS are listed, 42 of which are from the *B.P.* The only notable *B.P.* tablets not included are those of phenazone, and quinine bisulphate and quinine hydrochloride. From the *B.P.C.* are chosen many others—for example, A.P.C., aminophylline, phenobarbitone with theobromine, papaveretum, acetarsol, diphenan, and several purgatives. To these the *N.F.* adds its own quota to fill a number of gaps—for example, ammonium chloride (enteric-coated), amphetamine sulphate, calciferol forte, pethidine, and quinidine sulphate. Butobarbitone is now accompanied by new tablets of cyclobarbitone, hexobarbitone, methylphenobarbitone, and phenytoin sodium; cascara sagrada and ferrous sulphate are still present, the latter being in neither the *B.P.* nor the *B.P.C.*

Altogether 62 INJECTIONS (compared with only 8 in the earlier formulary) are given—mainly from the *B.P.*, which contributes 53 of its 75 preparations for injection. This wide and valuable range of modern drugs is supplemented by other injections, including those of amphetamine sulphate, benzocaine, morphine and hyoscine, paraldehyde, and sulphadimidine sodium.

The MIXTURES form a large group (44) which has a less modern appearance; only a single new one is added—mist. pot. cit. Among the 14 deleted many are archaic—for instance, mist. digit. *N.W.F.* Ingredients eliminated from formulæ, presumably in deference to pharmacological opinion, are tinct. opii camph. from mist. ammon. et ipecac. co., and tinct. nuc. vom. from a cascara preparation. Bitters, expectorants, and formulæ containing potassium bromide still occupy much space. It is difficult to imagine the indications for prescribing chloral hydrate gr. 5 and potassium bromide gr. 10 thrice daily. The dose of iron and ammonium citrate has been suitably increased, and the doses of tincture of colchicum have been amended. The amount of tincture of opium in mist. cret. aromat. c. opio has been doubled. The general instruction "To be taken three times a day" scarcely suffices for the main therapeutic uses of the mixtures which contain ammonium chloride, sodium citrate, and sodium salicylate respectively.

Of the less important preparations for internal use, few are listed. DRAUGHTS are again more strongly flavoured; but why does potassium bromide still accompany chloral hydrate in one of them? From the LINCTUS section heroin has been firmly removed. There are three new ELIXIRS, one containing ephedrine hydrochloride. The EMULSIONS are still almost all purgatives, and a few official purgative preparations have been added to the PILLS. The CAPSULES are mainly useful vitamin preparations not provided by the *B.P.* The POWDERS for use as antacids are unchanged, and bismuth preparations have been pointedly refused readmission since their deletion during the war. The VITRELLÆ (a new term, contrasting with CAPSULES, which are to be swallowed) are crushable and contain respectively amyl nitrite, octyl nitrite, and trichlorethylene.

The different types of local application far exceed in number those used for systemic effect. Their formulæ provide a very wide range of preparations, most of which are commendably simple; it is most convenient to have authoritative information on the composition of many minor medicaments such as lotions, mouthwashes, and dusting-powders, as well as more potent materials such as are used for germicidal action or local anæsthetic effect. The DUSTING-POWDERS are now designated "conspersi" to distinguish them from the PULVERES, which are taken internally. The varieties of preparation for use on skin surfaces number more than twelve. There are few changes in the LOTIONS or in the APPLICATIONS (concerned with treatment of infestation). Aminacrine is a gratifying addition to the SOLUTIONS, among which proflavine hemisulphate remains; the *B.P.* iodine solutions, lysol, and ether soap have also been added here. There are several new LINIMENTS and several new PAINTS, the latter including Castellani's paint and podophyllum in liquid paraffin. The section on PASTES is much larger than before. Half of the OINTMENTS are *B.P.* and there are no important omissions from that extensive list. Many standard *B.P.C.* ointments remain, and the formulary adds a compound cinchocaine preparation and an ointment of salicylic acid and sulphur.

Oral preparations (LOZENGES, PASTILLES) are increased in number, and include local anæsthetics. In the ear, nose, and throat sections the principal change is the elimination of oily vehicles for SPRAYS. New EYE LOTIONS include one with saline (1·8%) and one with sodium bicarbonate (3·4%). The EYE DROPS have several modifications and additions; the latter include mild silver protein, proflavine hemisulphate, and the new mydriatic lachesine. EYE OINTMENTS are mainly from the *B.P.*; two cocaine preparations have now been included.

Several new formulæ are included for ENEMATA, but the authors of the formulary have failed to retain the ox-bile enema. SUPPOSITORIES now include the two new hamamelis preparations from the *B.P.* The PESSARY of ichthammol was the only pessary listed in the *N.W.F.*; four additions have been made—acetarsol, lactic acid, silver picrate, and proflavine hemisulphate.

The infants section retains the well-known zinc and castor-oil cream. In the mixtures special care has been taken to make the medicines palatable. Some pædiatricians will no doubt question the value of preparations such as mist. calc. carb. co. pro infant. and mist. pot. brom. pro infant. There is a notable inadequacy in the doses given for cod-liver oil emulsion and for the tablets of ascorbic acid even for prophylaxis. Why not acknowledge the excellent formula of the cod-liver oil compound issued by the Ministry of Food? Doses of drugs for children of different ages are admittedly difficult to describe briefly, but the doses of alkali in the pot. cit. mixtures and of iron and ammonium citrate seem rather small. The continued prominence of hydrarg. c. cret. among the tablets will also disappoint many hospital pædiatricians.

The formulary, which has been adopted by the Ministry of Health, will come into force on May 1. No-one will welcome the new volume more heartily than the pharmacist, who naturally hopes that the N.H.S. practitioner will simplify the work of dispensing by using it whenever possible. For his part the practitioner, though not restricted to the contents of the formulary, can help to keep the costs of the pharmaceutical services within bounds by adhering to it whenever it contains a suitable prescription.

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Annotations

HANDOUTS FOR PATIENTS

THOSE doctors who are justly criticised by patients because "they don't tell you anything" are not always out to make a mystery: often they cannot spare the time to give the patient a detailed simplified account of the pathology of his condition; and rather than mislead him with a word or two they take refuge in silence. How can this difficulty be overcome to the patient's satisfaction but without further encroachment on the doctor's time? Dr. Charles Fletcher[1] suggests that, for patients with recurrent or chronic conditions, much might be done with simply written leaflets. As a pilot model he has drafted such a leaflet on the nature and treatment of dyspepsia, defined (though not in these terms to the patient) as "painful gastric or duodenal dysfunction whether due to peptic ulcer or other causes." This leaflet can be handed to the patient to take home and read; and at his next visit—Dr. Fletcher emphasises the importance of this—his questions about it can be answered quickly and clearly, without much tedious explanation.

The leaflet (which may be had from the *Practitioner* office[2]) begins with a brief account of digestion, illustrated by a diagram of the stomach and its associated organs. A paragraph on indigestion follows, and here we think Dr. Fletcher has been rather too informative, or perhaps has told the facts in too alarming a way. Is it wise, or is it unwise, to tell a patient of the "ulcer type" about the dangers of perforation and hæmorrhage? And, if he should be told, is it wise to use such phrases as "the stomach or duodenum gets digested right through," and "a blood vessel is digested away"; or to warn the patient that a severe hæmorrhage may lead to fainting or need treatment by transfusion? These are striking phrases which will stand out vividly in the mind of an anxious patient. The issue is difficult, for while some patients are over-anxious about their condition, others take refuge from fear in bravado, and refuse to take the slightest precautions. On the one hand, knowledge will encourage patients of the second type to do as they are told; on the other, it will scarcely promote—in patients of either type—the peace of mind on which Dr. Fletcher later puts so much emphasis. The sections of the leaflet which follow, however, will be generally accepted. He describes the ulcer diet and the regimen clearly and cleverly, explains the action and purpose of antacids, belladonna and olive oil, vitamins, and sedatives, gives good little homilies on rest for the mind and for the body, and ends with three detailed diets—strict; moderate, and convalescent.

The principle he has here outlined has long been applied by many doctors, who keep a stock of their own printed or multigraphed instructions to hand to suitable patients. Especially where explanations are attempted, such notes are by no means easy to write, and there is much to be said for using those produced by experts. It would be useful to many practitioners to have reliable tracts for distribution to patients with various chronic or recurrent complaints, such as asthma and hay fever, varicose ulcer, bronchiectasis, rheumatism, psychosomatic skin conditions, compensated or uncompensated heart-disease, hypertension, and diabetes. At the same time it should be remembered that many people absorb the spoken word more easily than the written—especially if it is well spoken by a doctor who takes pains to make his patient understand. A great deal of anxiety has been generated by patients reading about their maladies and getting the subject out of focus. Moreover in these mechanistic days we must keep watch against any tendency to standardise medicine, whether by directives to the doctor or by directives to the patient. Such handouts as Dr. Fletcher has devised should be used (as he insists) as an aid to, rather than a substitute for, frank discussion of his case with the patient.

1. *Practitioner*, 1949, **162**, 51.
2. From 5, Bentinck Street, London, W.1; at 6d. post free.

SURGERY OF INOPERABLE GROWTHS

THE place of ultraradical surgery in the treatment of so-called inoperable malignant growths has been much discussed. In this country, Gordon-Taylor, Grey Turner, and others have published reports of successful cases of multiple "eviscerating" procedures requiring skill, speed, and courage; but heroic procedures of this kind have usually carried so high a mortality-rate that many have deemed them unjustifiable, at any rate in less capable hands. However, the advent of improvements in anæsthesia, the use of the sulpha drugs and penicillin, and the simplicity of blood-transfusion have materially lessened the risks, and in our present issue Mr. Raven pleads for a more enterprising outlook on the surgery of advanced malignant disease, giving examples of its success.

About a year ago we commented[1] on the exenteration operations of Prof. Alexander Brunschwig, late of Chicago and now of the Memorial Hospital, New York City. Brunschwig claims little more than palliation for these extensive operations, and the advantages of such palliation have to be judged in relation to a primary operative mortality approaching 25% and some inevitable postoperative discomfort. An occasional "cure" goes far, of course, to justify such tremendous surgical undertakings; and some of Raven's results are certainly impressive. On the other hand, in a case sufficiently advanced to require Brunschwig's operation of hysterovaginectomy, total cystectomy, transplantation of ureters, and rectosigmoidectomy with what he calls a "wet" colostomy, it is likely that the lymphatic system will already be widely affected; and, unless one has faith in the ability of deep X-ray therapy to eradicate secondary deposits in abdominal lymph-glands, the prospects of "cure" are correspondingly poor. It has yet to be proved that for the survivors of such an operation life is prolonged, and (more important still) that life is less uncomfortable or more happy. The decision must rest largely with the patient: some people would prefer to be alive with severe disability, while others would not think the price worth paying. The fact that, without operation, the outlook is hopeless does not justify the surgeon—and especially the relatively inexperienced surgeon—in taking great risks, unless he believes that a successful result would be reckoned successful by the patient.

RICE AND HYPERTENSION

THE diet for hypertension popularised in the United States by Kempner[3] includes 250–300 g. of rice a day. No less than 95% of the 2000 calories in this diet is furnished by carbohydrate: otherwise it comprises 20 g. of protein (from rice and fruit) and not more than 5 g. of fat, 200 mg. of chloride, and 150 mg. of sodium. Fluid intake is restricted to 700–1000 ml. of fruit juice. This régime, which is a clever if somewhat dull blend of low-protein, low-sodium, and low-fluid diets, Kempner claims to be effective in the treatment of hypertension and cardiac œdema. Brams,[3] too, reports "excellent results . . . with the patient at work provided he coöperated faithfully"; while Contratto and Rogers,[4] of Boston,

1. *Lancet*, 1947, ii, 918.
2. Kempner, W. *N. Carolina med. J.* 1944, **5**, 125, 273; *Ibid*, 1945, **6**, 61, 117; *Ibid*, 1947, **8**, 128.
3. Brams, W. A. Treatment of Heart Disease. London, 1948; p. 135.
4. Contratto, A. W., Rogers, M. B. *New Engl. J. Med.* 1948, **239**, 531.

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say that it offers "the greatest hope so far for the medical treatment" of hypertension. A major difficulty seems to be that the régime does not commend itself to patients; for only 34 of Contratto and Rogers's 55 patients coöperated well enough for their cases to be included in the report. At the end of three months' treatment their blood-pressures had fallen on average from 210/120 to 158/100 mm. Hg; a "definite and persistent drop in blood-pressure" was recorded in 25 (70%). There was also a drop in weight of about 10–15 lb. in the first and second months, and all patients had a period of weakness, accompanied sometimes by severe mental depression, during the first few weeks. Apparently relief of headache, emotional tension, and nervousness was an outstanding feature of the response. There was also a pronounced fall in urinary chlorides (indeed this fall was estimated as a check of the extent to which patients were adhering to the diet); and lately Kempner et al.[5] have reported that substantially less phosphate and sulphate is excreted with this than with a "regular" diet or while fasting. Contratto and Rogers conclude that improvement is due to the low sodium intake. There is some evidence for this in a report by Rosenberg and his colleagues,[6] who found that of 7 hypertensives on a low-sodium diet 4 had a statistically significant fall in blood-pressure, while of 5 on a rice diet 3 had such a fall—though without relief of symptoms.

ADVANCES IN EPILEPSY

THE fight against epilepsy is progressing on many fronts. A better understanding of its history, new laboratory devices, and new methods of therapy, and a study of the ravages of war are all factors in the forward push. The report of a joint meeting of the Association for Research into Nervous and Mental Disease with the American chapter of the International League Against Epilepsy shows[7] how varied is the approach to the general attack. Thus it may be made through the investigation and classification of the various clinical forms of fit, through the study of cerebral anatomy and cerebral localisation, through evaluation of the acquired and genetic factors in ætiology, through electro-encephalographic (E.E.G.) patterns, through the physical and chemical changes underlying neuronic metabolism and their modification by drugs, or through the study of associated mental conditions and of social reactions. An outstanding feature is the growing knowledge of the electrophysiology of the nervous system. Its value in localisation is great, but it must always be remembered that E.E.G. aberrations are an accompaniment, and not a cause, of epileptic manifestations, and that the physical and chemical processes underlying the electrical abnormalities must be understood before the root of the matter can be reached. We may indeed yet return to the old concept of epilepsy as primarily a metabolic disorder. Perhaps we need to stop and reflect where all this new research is leading us. There is a place now for a book on epilepsy in the English language, embodying our recent advances in knowledge.

A volume[8] containing 15 papers on epilepsy read before the American Psychopathological Association deals mostly with psychiatric aspects of the complaint and their social implications. The case for a specific epileptic personality is considered, but the general conclusion is that there is little evidence to substantiate it.

5. Kempner, W., Lesesne, J. M., Newborg, B., Whicker, C. F. *Amer. J. med. Sci.* 1948, 216, 687.
6. Rosenberg, B., Rosenthal, A. E., Rosenbluth, M. B. *Amer. J. Med.* 1948, 5, 815.
7. Research Publications: Association for Research in Nervous and Mental Disease; vol. 26, 1947. Williams and Wilkins Company, Baltimore.
8. Epilepsy. Proceedings of the 36th annual meeting of the American Psychopathological Association, New York, 1946. Editors: Hoch, P. H.; Knight, R. P. London: Heinemann Medical Books. 1948. Pp. 214. 21s.

PSYCHOTHERAPY IN GENERAL PRACTICE

IN response to an obvious need, the Commonwealth Fund provided in April, 1946, at the University of Minnesota a short postgraduate course in psychotherapy for general practitioners. The number of those attending was limited to 25, and during the fortnight that the course lasted these doctors lived, along with their instructors, in the Centre for Continuation Study, a building designed for such purposes and including "dormitories, a cafeteria, a garage, classrooms and an ample lounge, all under one roof." The aim of the course was to accustom the practitioners to use essential psychiatric modes of thought in their approach to patients with neurotic and kindred disorders; the methods of instruction were clinical practice under supervision, coherent simple presentation of a few basic concepts, and abundant informal discussion. Much thought was given to the planning of the course, and a distinguished group of psychiatrists, with two general physicians, provided the instruction. The content of the teaching and a good deal of the method is now disclosed in a detailed report.[1] No-one who reads this can doubt the skill with which the teachers avoided the pitfalls in so ambitious and difficult a venture, or the success they attained—not, of course, in turning the practitioners into psychiatrists, but in enabling them to deal much more confidently and effectively with the emotional and other mental ills of their patients. The teachers uniformly avoided jargon and the use of concepts too abstract and involved or superficially improbable for their listeners' acceptance: much of the exposition is reminiscent of T. A. Ross's *The Common Neuroses*. An ounce of teaching such as this course afforded is worth many pounds of "psychosomatic" propaganda. The demands on the teachers, however, and the material requirements, are exacting. The account of how well these demands were met in the Minnesota experimental course is stimulating and informative.

THE NAVIGATION OF BIRDS

Two American ornithologists[2] took seventeen adult gannets from their nests, transported them rapidly 215 miles, and released them one by one a hundred miles from salt water; 63% returned to their nests, at an average speed of 99 miles per day (m.p.d.). This sort of experiment has often been done before; the figures for the swallow, for instance, were 67% and 141 m.p.d., for the herring gull 97% and 90 m.p.d. One of the most spectacular was the taking of a Manx shearwater from her nest off the Welsh coast to Venice, whence she made the return trip in fourteen days. What is peculiar about this experiment with gannets is that nine birds were followed after release at a discreet distance by the ornithologists in an aeroplane and their courses were charted. The results show that in every case the birds spiralled round after release, as though casting about for a clue to the way home. This is similar to the behaviour of homing pigeons. How do the birds find their way home? (Let it be firmly stated that we are not here concerned with migration, which is probably an instinctive process apart.) Many theories have been propounded—that they are oriented by the position of the sun as bees are; that they are guided by geomagnetic waves, though in fact they seem unaffected by a strong artificial magnetic field; that their semicircular canals are sensitive to the Coriolis force; that they have topographical memories; that they find their way in fog by infra-red vision. No doubt birds have

1. Teaching Psychotherapeutic Medicine: an Experimental Course for General Physicians. Editor: Helen Leland Witner, PH.D. New York: The Commonwealth Fund. London: Oxford University Press. 1948. Pp. 464. 21s.
2. Griffin, D. R. *Scientific American*, 1948, 179, 18.

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a different auditory and visual range from man, as dogs and most other animals have; but before we postulate a new sense organ are we sure that we have given due weight to the organs that we know exist? We insensitive human beings, who can detect one part of paraffin in ten thousand of soup, who can feel the difference between one and two layers of tissue paper, who can instantaneously calculate within 5° the direction of a noise by the unequal impacts on each ear (unless we are one-eared, when we lose all sense of direction of noise), who can smell land 80 miles out at sea—we who in spite of all this are insensitive in all respects compared with some animals, are we sure that we have given due credit to the sensitivity of that wonderful structure, the feather, as a tactile organ of winds and vibrations? The albatross doing his 20 knots without stirring a wing, the petrel darting down the concavity of a comber, are playing with the upward and oblique thrusts of air from the waters as a master on a musical instrument. It may well be that patterns of air movements characteristic of land outlines are discernible miles away by the feathers of birds and that the great winds have distinctive qualities undreamt of by man.

Two other points may be considered. One is the habitual animal practice which may be termed turning away from negative evidence and which accounts for the circular course taken from the point of departure. One can see this demonstrated by hunting dogs. Lost explorers who find themselves going in circles may be doing the same thing unconsciously. The other point is that a sense is often enormously increased by emotion. The poor gannets of this experiment are comparable to mothers torn from their children or small boys during their first days at boarding-school. As they circle round, looking for a clue that shall lead them home, in their minds is a near view of their glorious eggs, the feel of the stir of the chicks in their breast feathers, the dear old tang of excreted fish (which may well be sensed by the conjunctiva), the familiar outline of the headland. High above in the aeroplane circle the calculating and insensitive men.

FLY-BORNE DIARRHŒAL DISEASES

AN important field experiment on the part played by flies in the spread of diarrhœal disease has been completed in Hidalgo county on the Mexican border of Texas. In a summary of this work, which took nearly two years, Watt and Lindsay [1] say that the control of flies by modern insecticides caused a significant reduction in the large amount of infection, illness, and death due to diarrhœal disease in the area studied.

Hidalgo county contains nine small towns, which for the experiment were divided into two population groups each of about 35,000 people. The prevalence of shigella and salmonella infection in these two groups was measured by making at least 1300 stool-cultures every month from school-children under ten years of age. Notifications of morbidity and deaths from diarrhœal diseases were also recorded but were regarded as a less accurate measure of the prevalence of infection. A sampling method described by Scudder [2] was used to make a continuous record of the density of the fly populations. For the first sixteen months of the experiment D.D.T. spraying was used on a large scale in one group of towns to control flies, while the other group was left untreated; for a further six months D.D.T. was used only in the group of towns which had at first been left untreated. Soon after D.D.T. spraying was stopped in the first group and started in the second there was a reversal of the relative average densities of fly populations and also of the relative prevalence of diarrhœal infection and disease. First in one group and then in the other the application of D.D.T. appeared to reduce the number of flies and to diminish the prevalence of diarrhœa, especially that due to shigellæ; it had little effect on the incidence of salmonella infections.

The trial showed, however, that control over flies by an insecticide like D.D.T. is very temporary, for spraying had to be repeated frequently. This expensive procedure is thus best used as a temporary expedient or to supplement other measures such as the elimination of man-made breeding-places of the fly.

1. Watt, J., Lindsay, D. R. *Publ. Hlth Rep., Wash.* 1948, **63**, 1319.
2. Scudder, H. I. *Ibid*, 1947, **62**, 681.

MEDICAL ILEOSTOMY IN ULCERATIVE COLITIS

AMONG the various treatments tried in ulcerative colitis, each of which has its advocates and its successes and failures, the principles of rest and a suitable diet are agreed on by most physicians. Ileostomy is the most logical way of ensuring rest for the colon, and when it is performed early, while the patient's general condition is still good, it produces a considerable clinical improvement in a high proportion of cases. Understandably, however, patients are reluctant to undergo this operation and it is therefore usually done only as a last resort, with poor result. Machella and Miller,[1] of Pennsylvania, have tried to overcome this objection by means of what they term a "medical ileostomy." They pass a Miller-Abbott tube to a point just proximal to the diseased part of the colon and withdraw the residual fluid by constant aspiration. Periodic radiograms are taken to make sure that the tube is in the right place. It is retained until the quantity of fluid aspirated diminishes enough to show that intestinal absorption is almost complete and until the patient is improving clinically, as judged by his general condition and sigmoidoscopic appearances. The time taken for these signs of improvement to appear varies from 7 to 15 days. At the same time Machella and Miller have extended the concept of a low-residue diet by using a 50% 'Dextri-maltose,' 50% enzymatic protein hydrolysate mixture with added vitamins. This provides a high-calorie high-protein intake in a form which is almost completely absorbed. Any residue is in fluid form and can easily be aspirated via the tube. This diet is continued for a period depending on the patient's progress; in the present series it ranged from 7 to 52 days and was followed by a low-residue diet of the more usual form.

Of 12 patients treated on this régime, a remission was induced in 11, in 9 of whom the remission was still present after 2–12 months. All 11 patients were in useful employment. A further 12 patients were then treated on this diet without the tube and the results seem to have been as successful as in the former group. The Pennsylvania physicians deduce, therefore, that an easily absorbable, high-protein, high-calorie diet is probably the essential procedure for the immediate control of an attack. Whatever their treatment, most patients with ulcerative colitis have remissions, lasting in some cases for several years, and the number treated by Machella and Miller is too small for any definite conclusions to be drawn. But their lines of treatment are logical and promising and appear to be well worth trying in this enigmatic disease.

1. Machella, T. E., Miller, T. G. *Gastroenterology*, 1948, **10**, 28; *Amer. J. med. Sci.* 1948, **216**, 425.

Mr. ARTHUR BLENKINSOP, M.P., parliamentary secretary to the Ministry of Pensions since 1946, has been appointed parliamentary secretary to the Ministry of Health in succession to Mr. L. J. Edwards. Mr. Edwards, who now moves to the Board of Trade, has been at the Ministry of Health since 1947, and his transfer will be much regretted by many members of our profession who have come into contact with him.

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Special Articles

STREPTOMYCIN IN THE TREATMENT OF TUBERCULOSIS

AN OFFICIAL MEMORANDUM *

THE following is a provisional assessment of experience already gained in this and other countries in the use of streptomycin in tuberculosis. It is hoped that it may assist British specialists in deciding when and how to use the drug.

In meningeal and miliary tuberculosis, streptomycin is the most effective drug so far discovered. In some other forms it has a place in therapy, but must be considered only a useful adjuvant to other accepted forms of therapy, and does not in any way replace them. Evidence at present available suggests that in some forms of the disease it is of little or no value.

Two main obstacles—toxic effects and the emergence of drug-resistant strains of tubercle bacilli—limit the use of streptomycin at present. Much work yet needs to be done to find for each form of the disease the best scheme of dosage which will combine therapeutic effectiveness with low toxicity, and will delay or prevent emergence of resistant strains.

ADMINISTRATION OF STREPTOMYCIN

Recommendations under this heading must be tentative only. The standard route of administration is by intramuscular injection. For tuberculous meningitis the intrathecal route should also be used.

Dosage

For *miliary and meningeal tuberculosis* a daily intramuscular dose of 20 mg. per pound body-weight up to a maximum of 2·0 g. is recommended. Intramuscular treatment should be maintained for at least four months, and in some cases further courses may be required. In addition, for meningitis 50–100 mg. streptomycin dissolved in 5–10 ml. saline should be injected intrathecally daily during the first few weeks. The optimal frequency of intrathecal injection is not yet established, but it seems advisable in the average case to give intrathecal injections daily for the first three weeks and then every other day for two weeks. Further courses of intrathecal injection are probably necessary.

The course of tuberculous meningitis under streptomycin treatment is very variable, and may be complicated by spinal block interfering with intrathecal therapy. Among the many schemes of dosage that have been used the following are two examples:

(i) Intramuscular streptomycin during weeks 1–3, 5–7, 10–12, 14–16. Intrathecal treatment every day during the first week, and on alternate days during weeks 2, 3, 5, and 10.

(ii) Intramuscular streptomycin during weeks 1–12, 17–20. Intrathecal streptomycin daily during weeks 1–4, 9–12.

In *tuberculous conditions other than miliary and meningeal*, 2·0 g. daily was at first the usual dose for all adult patients but this produced toxic effects in most cases; 1·0 g. a day has been found to be less toxic, and is possibly equally effective; 0·5 g. a day is still less toxic, but its efficacy has not yet been fully established.

It may be more satisfactory to adjust the dosage to body-weight. As a general guide to dosage in both children and adults, 10 mg. per pound body-weight per day is suggested. Since toxic effects are more severe in older age-groups, the dosage should be lower for patients over the age of 45.

Frequency of Intramuscular Injections

The most recent evidence suggests that the maintenance of a fairly constant streptomycin blood-level by injection at frequent intervals during the day is unnecessary. The administration of the daily dose in 1 or 2 injections is recommended.

Duration of Treatment

No single scheme can be considered suitable for all forms of tuberculosis. According to present knowledge the maximal effect is reached within the first one or two months, and for most cases of other than miliary or meningeal tuberculosis it is useless and may be dangerous to treat continuously for more than three months. On the other hand, it is probable that treatment for less than one month is ineffective.

TOXICITY

Streptomycin, unlike penicillin, carries a risk of certain toxic effects. While the incidence of these has been reduced with improved drug purity and lower dosage, they cannot be ignored.

Vestibular damage.—This is the commonest toxic effect of streptomycin. It may be extremely disagreeable at its onset, but the initial symptoms do not last long, and the inconvenience to the bed patient is not serious. The damage to vestibular function is often irreversible but some degree of compensation occurs and unless the signs of dysfunction are sought the sequelæ may be overlooked, particularly in the later stages. They may be sufficiently serious to incapacitate a person, and prevent him from working at his normal occupation. Thus a person with vestibular damage from streptomycin therapy may become incapable of driving a car, walking steadily in the dark, or of crossing a congested street.

The danger of toxic effects increases with age and they occur with especial frequency after middle age.

Vertigo.—This most frequently begins in the fourth or fifth week of treatment. The subjective effects become progressively less after a few weeks as compensation occurs. Nystagmus or altered vestibular reactions are frequent and may occur even in the absence of subjective symptoms.

Visual upset.—Difficulty in reading is sometimes complained of during the early stages of vertigo, but is usually transitory. It is probably due to neuromuscular disturbance associated with the vestibular damage.

If vestibular symptoms appear, some degree of dysfunction may be permanent, and this danger should be weighed against the further improvement that might be expected from continuation of treatment. Careful watch should be kept for evidence of vestibular dysfunction. Tests such as the caloric reaction should be carried out where feasible, and in ambulant patients functional tests such as the Romberg test, walking along a straight line with eyes open and closed, or walking on a mattress.

Nausea, anorexia, and vomiting often begin during the third or fourth weeks. These symptoms may be quite severe, but are often relieved by administration of anti-histamine drugs, such as 'Benadryl' 50 mg. by mouth.

Local pain at the site of injection is seldom severe, but may be relieved by adding 0·5 ml. of 1% procaine to the volume of solution for injection. This is rarely necessary.

Sensitisation reactions.—Skin eruptions and pruritus sometimes occur in the early stages of treatment. These are usually relieved by administration of anti-histamine drugs. More severe skin complications are exceptional, but exfoliative rashes have occurred in a few cases; these do not respond to anti-histamine drugs and may

* By the streptomycin subcommittee of the Standing Advisory Committee on Tuberculosis to the Ministry of Health. The subcommittee's members are Sir ROBERT YOUNG (chairman), Dr. J. H. HARLEY WILLIAMS (secretary), Dr. A. S. HALL, Dr. D. P. SUTHERLAND, Mr. C. PRICE THOMAS, Dr. NORMAN F. SMITH (Ministry of Health), Dr. J. G. SCADDING, Dr. E. H. HUDSON, Dr. G. S. TODD, Dr. ANDREW MORLAND, Dr. N. LLOYD RUSBY, Dr. L. E. HOUGHTON, Dr. W. E. SNELL, Mr. A. L. D'ABREU, Dr. JAMES WATT, Dr. P. M. D'ARCY HART, and Dr. MARC DANIELS.

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necessitate stopping the streptomycim. Other evidence of sensitisation, such as drug-fever, occasionally accompanies the skin reaction.

Renal complication.—Albumin and casts have been found in the urine in some cases. With the moderate dosage at present used, these abnormalities subside without discontinuing treatment.

Serious neurological sequelæ due to meningitis should be distinguished from toxic effects due to streptomycin.

SENSITISATION IN ATTENDANTS HANDLING STREPTOMYCIN

Skin rashes have occasionally been noted among nurses responsible for giving streptomycin injections, usually after several months. An eczematous reaction has occurred on the fingers, the flexures of the elbows, and around the eyes. The latter has often been the most obvious site, and that which has caused the first complaint. Improvement has been rapid when contact with the drug has ceased.

In view of this risk it is advisable that attendants should wear rubber gloves while handling streptomycin and should wash their hands after removing the gloves.

STREPTOMYCIN RESISTANCE

Streptomycin as used at present very commonly leads to the emergence of drug-resistant strains of tubercle bacilli. This event not only limits the duration of an effective course of therapy but may spoil the patient's chances should a second course be required, or the drug needed for a recrudescence or a fresh lesion at a later date.

This eventuality must be borne in mind in planning treatment. A long-term plan of treatment should be made; in this a course of streptomycin can only be a part, and *one which can probably not be repeated effectively*. The position may change if combination with other drugs or some other scheme of administration is found to postpone or abolish the emergence of resistance and to be therapeutically effective.

If the drug is indiscriminately used, particularly in advanced cases with copious sputum, resistant strains will be disseminated, and could give rise to cases of tuberculosis which may not respond to streptomycin. In order to detect dissemination of resistant strains, at the start of treatment in any particular case, material if available should be collected for culture, and the bacilli isolated and tested for streptomycin sensitivity.

INDICATIONS

The facts given indicate the importance of resisting pressure to try the effect of this new drug in all the many forms of pulmonary tuberculosis.

In the present state of knowledge, the simplest general criteria for selecting cases for streptomycin might be as follows: "Pulmonary tuberculosis in which the lesions requiring treatment are of recent development, progressive, and *unlikely to benefit from conventional methods* (e.g., bed-rest and/or collapse therapy) *alone*." This definition would include rapidly advancing pulmonary tuberculosis in which immediate collapse therapy would be dangerous or impracticable, and acute "spreads" including those after collapse therapy. It would exclude old chronic fibroid or fibrocaseous lesions; apparently terminal conditions; or minimal early lesions with favourable prognosis. Clearly the limitations are not stable and will undoubtedly be modified as further experience and trials of experimental nature outside them accumulate.

It should be remembered that in cases improving under streptomycin therapy it is usually recent lesions which show radiological clearing, that this clearing is rarely complete, that important cavities rarely close with streptomycin alone, and that relapses are frequent after first improvement.

Streptomycin should not be used as the only therapeutic measure in pulmonary tuberculosis. Indeed its major rôle may be to make possible the use of collapse procedures which, in its absence, would have had to be delayed or never performed.

Miliary and Meningeal Tuberculosis

Streptomycin therapy has reduced the very high mortality in these forms of the disease. Every diagnosed case should be treated, but treatment of meningitis is difficult and prolonged, and miliary cases may be complicated by meningitis even while under streptomycin treatment. For these reasons streptomycin should be given only in hospitals with the best facilities. Late relapses are frequent. Knowledge regarding best methods of administration is still very incomplete.

Ulcerative Tuberculosis of Larynx, Trachea, Bronchi, Tongue, and Pharynx

Streptomycin is of proved value in these conditions. In laryngitis and tracheobronchitis diagnosis should be confirmed where possible by laryngoscopy or bronchoscopy before treatment is started, and the examination should be repeated during and at the end of treatment in order to provide full assessment of the effects of streptomycin therapy. No additional advantage is apparently derived from giving streptomycin by methods other than intramuscular.

Thoracic Surgery

Prophylactic use of streptomycin to "cover" routine thoracoplasties, in the hope of decreasing the incidence of postoperative spreads, is not recommended on present knowledge. It should be reserved for the treatment of spreads when they actually occur.

Prophylactic use of streptomycin before and after resections of the lung for pulmonary tuberculosis is probably of value, but the best scheme of dosage for this purpose is not yet established.

The value of streptomycin injected locally into infected subscapular spaces after thoracoplasty is established. Systemic treatment in addition to local may be of value.

Cutaneous Sinuses and Fistulæ

Streptomycin often produces healing in tuberculous cutaneous sinuses and fistulæ. Local treatment in addition to systemic may be of value.

Tuberculosis of Alimentary Tract and Peritoneum

Favourable results have been reported in these conditions. Symptomatic improvement may occur rapidly but relapses are frequent, and the ultimate prognosis depends on the extent of lesions in other parts of the body.

Genito-urinary Tuberculosis

Streptomycin may prove of benefit in some types of genito-urinary tuberculosis.

Bone and Joint Tuberculosis

A few encouraging results have been obtained, but these are far from conclusive, and streptomycin treatment here too cannot replace standard therapy.

CONCLUSION

The above recommendations are provisional and will require modification as further experience accumulates. Much research is yet required to provide answers to some of the questions raised; participation in group investigations will add value to the work done in separate hospitals. The drug should only be used where full laboratory and X-ray facilities are available, and it is desirable that cultures to be tested for sensitivity to streptomycin should be made at the beginning, during, and after treatment. It is certain that indiscriminate use of streptomycin carries with it definite dangers both to the

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individual and to the community. The tendency to "try" this drug in every form of tuberculosis is to be condemned. Each single case should be considered on its merits; the assessment should take into account prognosis without streptomycin therapy and a weighing of the dangers of streptomycin treatment as against the possible advantages to be derived. If it is decided to administer streptomycin, then, with a realisation that probably only a single effective course may be given, an estimate should be made of the most suitable date for instituting streptomycin therapy within a long-term plan of treatment.

FOOTNOTE

Streptomycin is generally supplied in one of three forms—as the hydrochloride, as the sulphate, or as a calcium chloride double salt. Since a mixture of the sulphate and the calcium chloride complex in the test-tube produces a precipitate of calcium sulphate it is recommended that a change-over from one of these two salts to another in intrathecal administration (and probably also in intramuscular administration) should be avoided; if a change has to be made it is recommended that several weeks elapse between the last injection of the one salt and the first injection of the other.

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MEDICAL STATISTICS OF THE ARMY

Report on War Years

As long ago as 1861 a departmental committee recommended that the Army Medical Department should have a central statistical branch. Its purpose, it was suggested, should include the development of general vital statistics with a view to estimating major sources of wastage and clarifying (1) the relation of environment to the ætiology of disease, and (2) "the effects of treatment on the fatality and on the duration of diseases." The wisdom of these recommendations, then over half a century old, was heavily underlined by the war of 1914–18; and yet it was not until the start of the late war that, with the Army Council's authority, the director-general of the Army Medical Services set up a new statistical branch.

The immediate preoccupation of this branch was to meet War Office commitments to the Ministry of Pensions, and to supply information about hospital accommodation in the new situation resulting from the creation of the E.M.S. The aims became wider with the transference of the branch's work, as a temporary expedient, to the directorate of biological research, under Brigadier F. A. E. Crew, F.R.C.P., F.R.S. Afterwards this became the directorate of medical (statistical) research; and the work is being continued in peace-time by a permanent nucleus of experts, operating as a branch of the directorate of hygiene.

Part of the directorate's work is recorded in a report[1] issued last week. In an introduction Prof. Lancelot Hogben, F.R.S., to whom is due much of the credit for the Army's success in this new venture, observes:

> "Such a statistical machine, subserving the purposes of an all-in system of social medicine, can provide materials for the exploration of fundamental problems of medical science and can be an asset to the nation as a whole. The creation of a national health service, which will doubtless enlarge the scope and opportunities for more widespread use of statistical controls in medical research, will also demand solution of administrative problems for the solution of which Army experience may well serve as a preview and as a model."

But he adds these warnings: first, that for accurate analysis the statistician must be in day-to-day contact with the machinery for issue and assembly of documentary material; and secondly, that for full use of this machinery there has to be close integration between clinicians appreciating the possibilities of statistical procedures and statisticians alert to the biological significance of their subject matter.

PRISONERS-OF-WAR

The report, dealing mainly with the years 1943–45, opens with a section on total wastage of personnel, which shows that in each of the two years 1943 and 1944 disease alone brought about an annual loss of 2% of the total strength in both military and A.T.S. personnel. In males disease accounted for more than 95% of all medical discharges in 1943, and more than 80% in 1944. In each of the two years psychiatric disorders accounted for between one-third and two-fifths of all discharges with respect to disease among military personnel; while peptic ulcer, tuberculosis, and bronchitis together contributed more than one-fifth.

Former prisoners-of-war discharged up to July, 1946, are dealt with under two headings—repatriated and liberated. Of discharges due to disease in those repatriated from Europe, a quarter were due to tuberculosis, more than one-fifth to psychiatric disorders, and more than one-tenth to peptic ulceration; among those liberated tuberculosis was twice as often the cause of discharge as in the residual Army population.

With prisoners from the Far East the picture was very different. Malaria alone accounted for one-third of all discharges with respect to disease; beriberi accounted for 9%, and other deficiency diseases for 4%. Optic neuritis (here including retrobulbar neuritis and optic atrophy) made up 5½%, and defects of the field of vision a further 2%. Amœbic dysentery, other forms of dysentery, and oriental sore each contributed 2½%. Even such high figures do not give full weight to the importance of these diseases as causes of discharge, since they are based on the first recorded diagnosis only. Taking the second diagnosis into account, malaria was cited in 41% of discharges, beriberi in 18%, and other deficiency diseases in 8%.

HOSPITALISATION

A study of hospital admissions in the United Kingdom in 1943 shows that 6% of sickness cases were psychiatric disorders, while tonsillitis and gonorrhœa each accounted for 5%, hernia for 4%, and bronchitis for 3%. Accidental injuries amounted to one-seventh of all hospital admissions. As regards man-days in hospital, the leading causes were hernia (10%), psychiatric disorders (8½%), and internal derangement of the knee and appendicitis (4% each). Among A.T.S. the principal causes of admission through sickness were tonsillitis (8½%), appendicitis (6%), and psychiatric disorders (4%); and the main causes of loss of days through hospitalisation were appendicitis (9%), and tonsillitis and psychiatric disorders (6% each).

Of all patients admitted through sickness in 1943, about half were treated exclusively in military hospital, and a quarter in E.M.S. hospitals, while a quarter involved transfer to British Red Cross Society auxiliary hospitals or convalescent depots, or movement between military and E.M.S. hospitals. (A later section shows that at Dec. 31, 1945, the R.A.M.C. was operating altogether 14,871 beds in the United Kingdom.) The evidence

1. War Office: Statistical Report on the Health of the Army, 1943–45. H.M. Stationery Office. 1949. Pp. 294. 20s.

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suggests that the average stay in E.M.S. hospitals was about 25% longer than in military hospitals.

On average each soldier in the United Kingdom spent nearly 11 days per annum (or 3% of his time) in hospital and convalescent depot—8½ days on account of disease and 2¼ days as a result of accidental injury. Corresponding A.T.S. figures were 5 days for disease and ½ day for accidental injury. Taking into account retention in all medical units, including reception stations, disease and accidental injury accounted annually for an average of 12 days lost to a soldier and 8 days to a member of the A.T.S.

OVERSEAS THEATRES

An analysis of morbidity in the Middle East during 1943 and 1944 reveals that diseases of the ear, nose, and throat were collectively responsible for about 15% of all hospital admissions and about 10% of all man-day wastage. Bacillary dysentery, malaria, sandfly fever, and pyrexia of unknown origin also ranked high as causes of morbidity and wastage. With the exception of diphtheria, poliomyelitis, and infective hepatitis, the *rank order* of mortality from non-tropical diseases was fairly similar to that in the United Kingdom, with tuberculosis, neoplasms, and pneumonia at the top.

A survey of illness in West Africa between 1941 and 1944 shows that in European troops the major diseases were malaria and blackwater fever, dysentery, and venereal disease; and in Africans venereal disease, pneumococcal infections, chickenpox, yaws, and tuberculosis. The impressive progress towards the control of malaria is reflected in the fall of its incidence among British troops from 900 per 1000 per annum in 1941 to 90 per 1000 in 1945.

SURGICAL CASUALTIES

In the Normandy campaign, between June 6 and Aug. 1, 1944, wounded totalled 31,207, while the number dying from wounds in this period was 1780. In June 18,034 were evacuated, and in July 23,608. Of all injuries in these two months about 10% were trivial, 10% lethal, and 80% medium and severe (evacuated). As to the site and effect of wounds, these conclusions emerge:

1. Head and neck wounds were less likely to cause long-term hospitalisation, though relatively important as a cause of death.

2. Trunk injuries were about as common as head and neck wounds, but made by far the largest contribution to death from wounds.

3. Under 1% of arm wounds proved fatal.

4. Nearly two-thirds of long-term hospital cases were either leg injuries or multiple wounds; but there were relatively more slight leg injuries and more lethal multiple injuries.

5. Nearly 30% of casualties evacuated as a result of injury were due to multiple wounds, over half of which had only two wounds; about 5% of all injured received more than four wounds. Seemingly, patients with multiple injuries spent longer in hospital than those with single wounds.

6. With one exception there was little difference with reference to distribution of wounds by site among the different arms of the Service. Among troops serving with armour about 40% of hospitalised wounded, as opposed to under 30% for other arms, had multiple injuries.

7. Among single wounds about 15% involved bone injury; and such injury greatly increased liability to long-term hospitalisation.

8. Among single injuries bone injuries of the arm were relatively commoner than bone injuries of the leg.

9. Burns, which accounted for under 3% of single injuries, were most common on the arm.

With regard to weapons and wounds the following are among the main conclusions:

1. About 90% of all wounds were due to shells, mortar bombs, and gunshot (in about equal proportions). There was no dramatic difference with reference to relative severity of wounds caused by different weapons, except that bomb and gunshot wounds tended to produce a higher proportion of fatal injuries.

2. With respect to anatomical sites, the main difference between weapons concerned the propensity for inflicting multiple wounds. Gunshot wounds of the head and neck and trunk were relatively rare among evacuated injuries and relatively common among lethal ones—a fact probably referable to greater missile velocity.

3. Nearly 80% of gunshot wounds were single injuries, whereas under 70% of any other type were such. Pepperpot injuries were relatively most common from mines and grenades.

4. Assessed by downgrading, gunshot wounds appeared to cause more damage than other types.

MAJOR SOURCES OF WASTAGE

A detailed study has been made of the most important sources of wastage.

Hernia.—After about 1 out of every 8 primary operations the original condition reappears within twelve months. The overwhelming majority of such recurrences are the result of an operation "for the performance of which a relatively modest level of professional skill is perhaps too commonly deemed to suffice."

Perforated Peptic Ulcer.—Fatality in the United Kingdom between 1942 and 1944 was about 6%; the main causes of death are peritonitis and hæmorrhage. Gastric ulcers are about twice as liable to perforate as are duodenal.

Internal Derangement of the Knee.—This is a major source of wastage, mainly because of the high proportion of cases treated surgically and the long duration of treatment. Football is the most important cause contributing to the trauma, accounting for half of the Army cases. Of itself, excessive anteroposterior movement of the knee-joint is not a reliable sign of rupture of the cruciate ligaments. Of patients who underwent subtotal meniscectomy in the series under review, a trivial proportion required subsequent arthrotomy on account of symptoms attributable to meniscal remnants. Consequently the data appear to justify the practice of subtotal meniscectomy.

Jaundice Associated with Syphilis Treatment and with Blood-transfusion.—During the first half of 1943 the incidence of jaundice among patients undergoing long-term arsenotherapy (mainly in the United Kingdom) was about 45%. After the introduction of improved sterilisation procedure the incidence declined sharply; and during the period of decline the incidence of arsenical dermatitis remained constant. In addition a group of overseas patients treated with penicillin exhibited a high incidence of jaundice ($20{\cdot}2 \pm 3{\cdot}6$). "Arsenicals therefore play no significant part in influencing susceptibility to jaundice." Maximum susceptibility to jaundice appears to be in the very early stages of syphilis. The icterogenic agent of jaundice in syphilitics is probably identical with that of homologous-serum jaundice, but is certainly not that of infective hepatitis.

In a group of 462 patients evacuated from the British Liberation Army who received transfusions a six-month follow-up showed: (1) that of 248 patients transfused with whole blood alone, 0·81% developed jaundice; and (2) that of 214 who received plasma, either alone or with whole blood, 5·14% developed jaundice.

THERAPEUTIC MEASURES

In the final section, dealing with the efficacy of therapeutic measures, comparative results of treatment of syphilis with arsenicals and with penicillin, though based on data obtained before the importance of the K fraction was recognised, "at least emphasise the need for long-term follow-up before replacing arsenotherapy by penicillin."

From the report emerges much that has a direct bearing on civilian practice; from it, too, come occasional glimpses of conditions in civilian life. It is disconcerting to be reminded that in the second quarter of 1944 no less than 1 in 3 of all girls entering the A.T.S. had pediculosis capitis.

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The Wider World

NUTRITION AND HEALTH OF CHILDREN IN FIVE COUNTRIES OF SOUTH AMERICA*

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1. Paraguay

SINCE the breakdown in 1865 of the dictatorships which ruled the republic in its early days, Paraguay has found no stable system of government. Civil wars, foreign wars, and revolutions have followed each other with devastating regularity, and in these conditions it has been impossible to build up any regular Civil Service. A change of government means not only a change of ministers and a change of policy but also a change of most heads of departments and many subordinate technical persons. For instance, in the health services, the accession of a new party to political power may make it expedient for even such minor officials as sanitary inspectors to retire into temporary exile. So an important proportion of the small republic's limited technical skill is always in exile in neighbouring countries. Thus it has been impossible hitherto for any government to carry out comprehensive health programmes.

The modern Paraguayan is of mixed origin. His ancestors were for the most part Guarani Indians and Spanish conquistadores. All over the Americas, Indians and Spaniards have fought each other, and in Paraguay their struggles resulted in the destruction of both races: today the people are neither Indians nor conquistadore, but Paraguayans. Their language and customs are of as mixed a European and Asiatic origin as their features. The country has also proved able to assimilate newcomers quickly. It is remarkable how British and German immigrants lose much of their original nationality in the second generation and have become completely Paraguayan in the third—only a grotesquely mispronounced surname betraying their origin. A result is that Paraguay, almost alone among nations, has a tropical people without a colour problem—a fact that gives grounds for a sober long-term optimism.

Another important factor in shaping modern Paraguay was the war against the Argentine, Brazil, and Uruguay in 1865–70. So stubbornly did the Paraguayans defend themselves that when defeat came only 25,000 males are said to have been left alive and most of these were either young boys or old men. At the end of the war females are said to have outnumbered males by 10 to 1. In such circumstances neither Church nor State could hope to maintain monogamy, and family life broke down. The process was repeated on a lesser scale in the Chaco wars of 1930–35, in which 100,000 men (perhaps about a fifth of the male population) are believed to have lost their lives, and family life has never recovered from these disasters. Thus in the short period in 1940 for which there are published figures, 57% of births in Asunción were illegitimate, and in the country districts the proportion would be much higher. All my informants agreed that many men and women show no sense of responsibility toward children, and the lack of a stable home life is undoubtedly the most important adverse factor in child health in Paraguay today.

Intelligent guesses put the population at 1–1½ million, which is far less than the country could support: a recent survey by the Institute of Inter-American Affairs Food Supply Division (STICA) indicated that only 0·82% of the land was under cultivation. The countryside around Asunción resembles many parts of tropical Asia; but the scarcity of people, and perhaps especially of children, provides a remarkable contrast with the rural scene of India, for example. Obviously a million or so people in a backward agricultural community cannot afford all the paraphernalia customary in a modern State, and in the realm of administration the lack of numbers is obvious. Thus the department of health has a large and elaborate scheme of health supervision, but there are neither the men to fill the posts nor the money to pay what men there are. In these circumstances one doctor often has to fill several different government technical posts and at the same time support his own family by private practice. Efficiency is impossible in these conditions. Paraguay is in urgent need of several million more people.

There are two small minorities, not yet mentioned.

The first are the Chaco Indians. I was able to visit a small encampment of these in the Chaco just across the Paraguay River from Asunción. These people are hunters, with no knowledge of agriculture. They were living in grass huts in appalling dirt and squalor, for the most part destitute of clothing, but possessing a great variety of paints and feminine make-up. The women were engaged in primitive weaving or preparing food, of which there were large quantities in the camp. The food consisted of mixed roots and fleshes. The men had just killed a number of monkeys, which they were preparing to eat with relish. Apart from a great deal of superficial sepsis, the children looked strong and well. There are said to be between 10,000 and 20,000 of these Indians hunting in the Chaco. They have no affinities with the Paraguayans and their future must be very uncertain.

The second minority group are the Mennonite and Hutterite communities. These are recent immigrants of European origin, predominantly British and German. Their aim is to set up simple self-supporting agricultural communities, based on pre-ecclesiastical Christianity. Within their colonies they practise a complete communism. There are some thousands of Mennonites and 500 or more Hutterites. Talking to some of the leading Hutterites in Asunción I found them anxious to recruit children from Europe. They were enthusiastic, energetic, and well educated, and in a country with the potentialities of Paraguay such men should have a future.

FOOD RESOURCES

This section is based on parts of the STICA survey (to be published shortly) and on information gained in conversation.

The *staple food* is the root mandioca. It grows freely with a minimum of cultivation. There is plenty of land, and the Paraguayan need never be without enough food. Sweet potatoes are also grown in large amounts.

Cereals.—Maize is the most important crop. Small amounts of rice and wheat are harvested, but apparently none of the millets which are such valuable nutritious crops in tropical Africa and Asia.

Pulses and Beans.—A considerable variety of these are grown, mostly as cattle food.

Vegetables.—Very few are grown; indeed, large amounts are imported from the Argentine. But in the large vegetable garden attached to the Tuberculosis Sanatorium I saw a great variety of both tropical and temperate vegetables. Clearly production could be greatly increased with a little energy and instruction.

Fruits.—The long avenues of orange trees, heavily laden with fruit, are a feature of Asunción. Throughout the country oranges, mandarines, peaches, mangoes, and bananas grow in abundance.

Meat.—Huge herds of cattle are kept, and large amounts of beef are exported. In the capital itself ample meat is available at low prices. In the country districts all classes probably have a regular but limited supply.

Milk.—Despite the enormous number of cattle, little milk is produced. The wealthy in Asunción use imported tinned and dried milk. STICA has a small dairy farm, which brings into the capital 600 litres of clean milk a day, but there

* I visited South America in July, August, and September, 1948, as a consultant on behalf of the United Nations International Children's Emergency Fund (UNICEF). The views and conclusions expressed here are purely personal and do not necessarily reflect the views of the Fund.

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is no other private or government venture to compare with this small herd. The almost total absence of dairy cattle is astonishing.

Eggs.—The STICA survey records a production of nearly 8 million dozen eggs a year, produced by over $2^1/_2$ million farmyard birds.

Fish.—No attempt seems to have been made to organise fishing in the huge rivers.

Sugar-cane is grown throughout the country. The 1946 crop was reported to be over 13 g. million kg. This represents a per-capita supply for the year about one-third of that in Great Britain for the same year. Production could be increased.

Fats.—With the absence of dairy cattle there is practically no butter. The chief cooking fat is cotton-seed oil, but ground-nut oil is also used.

Beverages.—The principal drink is the locally grown tea, yerba mate, of which great quantities are drunk. The main alcoholic beverage is a locally made rum. The Paraguayan has not attained a reputation as a heavy drinker.

In summary, it may be said that the over-all food situation is not bad. Ample mandioca is available to supply caloric needs and there is enough fruit and beef to prevent signs of deficiency diseases. The diet is far from ideal and could be improved by higher consumption of vegetables, fish, sugar, and milk, all of which could be produced in the country. Of these, milk is the most important.

A real difficulty in developing food-supplies is the lack of a good transport system. Paraguay, a country larger than Britain, has only one motor road and one railway line. Transport is chiefly by bullock-cart, and the tracks are described for the most part as barely "jeepable."

DISEASES

For the first six months of 1940, records of births and deaths (with diagnosis) and also of hospital admissions were obtained. (After the change of government in that year it was impossible to keep up this programme.) Notifications were clearly very incomplete in the country-side, and the Asunción figures are of little value for comparative purposes, because estimates of the size of the population vary by 50%. The report does, however, suggest a high infant-mortality rate and a high incidence of infectious diseases. Thus out of 2277 deaths in which a diagnosis was recorded 552 (24·2%) were in infants under one year of age and 715 (31·4%) were from infectious diseases. Corresponding percentages for Scotland in 1945 were 7·6 and 8·1. The following account is perforce based on impressions gained from doctors and not on accurate statistical data.

Nutritional Disorders.—Gross undernutrition is seldom seen: a sufficiency of mandioca, and a little beef, is available for even the poorest. Similarly the deficiency diseases so prevalent in many tropical countries are not common. The high infant mortality and the large proportion of deaths from infectious diseases suggest that qualitatively the diets of large sections of the population may be inadequate, and casual observation suggested that the growth and development of many children falls far below their potentialities. However, the nutritional condition of the children appeared infinitely better than that of millions of children in other countries in the tropics.

Intestinal Parasites.—These, especially hookworms and roundworms, are a frequent source of ill health and poor development among children. The primary causes are absence of privies and widespread fouling of the ground in the vicinity of the houses, the marshy and muddy nature of the soil in the wet season, and the scarcity of footwear. In 1923–28 the Rockefeller Foundation carried out an intensive campaign against hookworm: large numbers of privies were constructed and many thousands of persons received vermifuges. The campaign had a great effect in improving the health of the people. Indeed, one observer held that it enabled a generation to grow up sufficiently strong to fight and win the last Chaco war. The direct effects of the campaign might be expected to last for 50 years. It has not proved possible to maintain installations properly and the degree of infestation is probably rising, though by no means so high as 25 years ago.

Venereal Diseases.—With loose standards of family life, syphilis and gonorrhœa are common. The congenital manifestations of syphilis are frequent. Of the women attending the antenatal clinic at a health centre in Asunción 1 in 5 have positive Kahn reactions.

Tuberculosis.—The incidence is high. It is the custom of the country to boil all milk, and little tuberculosis is of bovine origin. The death-rate from pulmonary tuberculosis in Asunción is probably not less than 200 per 100,000 persons.

Leprosy is also common and perhaps as many as 0·5% of the population are leprous. The treatment and care of these people, many of whom are children, and their segregation when necessary, are problems that are being tackled under great difficulties.

Malaria.—Most people said that malaria was bad in certain parts of the country, but in most districts the incidence was light.

Smallpox is common, but is of the mild alastrim type, rarely causing either death or blindness.

CHILDREN'S SERVICES

A very full scheme for children's services exists in the ministry of health. The resources of so small and disturbed a State are clearly insufficient for implementing the whole scheme, and it was impossible in a short time to judge how much was being done. The maternity and child-welfare department is responsible for antenatal clinics, for State homes for orphans, and for kindergartens. A school meals service was started in 1940 but had to be abandoned, and no meals are now being served in schools. There is a school medical service in Asunción with a clinic staffed by two part-time doctors. There is also a school dental service. It has been almost impossible to extend these services to the countryside, and even in Asunción their functioning is erratic. Last year some of the heads of departments of the ministry of health were operating at the front line in the war of the time.

SUMMARY

Paraguay is a small isolated tropical country. The general level of nutrition of the people is far from ideal and there is a high incidence of many infectious diseases. Nevertheless, the physical condition of the people is probably not so bad as that of millions of inhabitants of other tropical countries. This is due to the fact that the country is underpopulated. There appears to be a shortage of people, not of land.

"... If you only want to teach a nurse to make beds, use thermometers and record temperatures, learn the use of mackintoshes and drawsheets, administer douches and enemata and so forth, it seems absurd to devote three or even two years to the purpose. Any intelligent girl can learn it in six months, as those private hospitals which have to depend on untrained personnel have found abundantly. If on the other hand, you are wanting a woman who can take responsibility ... then it is absurd to talk of shortening the training course at all.... Actually of course you want both of these things. But do you want them both necessarily to be combined in every nurse? I think not. And I would base my plan for the training of nurses in the future on the further assumption that you will want a large number of girls for the first purpose, ministering to the patients' comfort, and a smaller number more highly trained for the second—partnership with the medical staff in the observation and treatment of patients.... In the merchant marine ... a man enters ... by taking employment as a seaman or cadet, and sits successively for his various 'mates tickets' and finally for his master's certificate. If that service were put on the same basis as present nursing training we should demand of every seaman that he should have his master's certificate in three or four years, and if he failed to get it he must leave the sea. That suggestion is of course ludicrous. I suggest it is equally unnecessary and wasteful in the case of nurses."—Dr. ARTHUR E. BROWN, *Hospital Magazine* (Australia), May, 1948.

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Disabilities

23. DUODENAL ULCER

I was only eighteen when I had my first attack of duodenal ulceration. Of course at that time no such diagnosis was considered by our excellent family doctor; nor, I imagine, would it have been entertained by the learned consultants of that day had I been referred to any. For even to them the lesion was a comparative rarity, and the idea that so young a subject could be afflicted would have been dismissed as preposterous. It was sufficient therefore to talk vaguely of "indigestion"; and, since my attack more or less coincided with participation in a friend's coming-of-age celebration, to regard it as a just retribution. But looking back I can recognise that attack as of textbook pattern. The pain came with clock-like regularity three hours after meals and was relieved by food. I recall how instinctively I resorted to effervescing drinks. I had a vague idea that in this way "acidity" was neutralised, though I appreciated that I had in fact provided no alkali. Now I recognise the influence of the gas in distending the pyloric antrum, which is a responsible factor if not the only one in relieving the pain.

The next attack occurred twelve months later during a holiday at the seaside in early spring. This time I attributed the "indigestion" to change of diet and exposure to cold winds. I may have been right, for there is evidence of a seasonal incidence; but more important, in all probability, was an antecedent period of worry, overwork, and anxiety in relation to an examination.

This sharp and protracted attack had a serious consequence. I now became preoccupied with my health and particularly with my alimentary canal. Apart from occasional pain, I was rarely free from abdominal consciousness; and since I often experienced discomfort two to three hours after lunch I invariably provided myself with biscuits or chocolate in case tea was not forthcoming. I received little help or sympathy. I must have been regarded as a troublesome young hypochondriac and I was fobbed off with a prescription which always incorporated bromide, accompanied by fatuous admonitions to "avoid indigestible food." My timid conjecture that I might have an ulcer was rejected by all my advisers, sometimes soothingly, sometimes contemptuously.

I experimented with diets. I resorted to patent medicines, seduced by the advertisements rich in promise and specious in the stories of satisfied customers. I will admit if not to neurosis at least to introspection; but was that surprising?

Towards the end of the summer I enjoyed a completely eupeptic month. This coincided with some régime or other that naturally was regarded as responsible. But in early autumn I had my third and most severe attack. I must have been a pathetic object. Not yet twenty, I ought to have had the joie-de-vivre to a superlative degree, and been completely unconscious of any physical disadvantage. Instead I was a hyperconscientious ambitious young man, with a metaphorical heart-ache and an only too literal stomach-ache, struggling to sustain a reputation.

At that time physical culture became fashionable. "Titan's system" (let us call it), with its schools all over London, widely advertised the assurance of strength to the would-be athlete and perfect health to the ailing, whatever their trouble. Of course dyspepsia loomed largely in the list of curable disabilities.

> If you can't digest that steak,
> A course of Titan you must take.

I took my first lesson in unremitting epigastric pain. Next day immediately after lunch I was seized with a tearing agony throughout the whole abdomen. I struggled to the railway station; with board-like abdomen I could just gasp out a request for a ticket to my home, an hour's journey from London.

This was clearly a perforation, presumably a small leak sealed by adhesions which had formed in anticipation. Yet all the treatment I had was less than a week in bed on peptonised milk, and within a fortnight I had begun to resume activities, fretting over the leeway to be made up.

* * *

I need only summarise the ensuing 45 years. Intervals of well-being with relapses of variable duration; but mercifully, with increasing age the attacks have become shorter and less severe. A remarkable feature has been the abrupt spontaneous termination of a long period of acute ulceration to be succeeded by complete alimentary tranquillity. It is rarely difficult to isolate some circumstance which has provoked a relapse, but the remission always seems inexplicable. If any particular treatment had been tried immediately before a remission it would certainly have received undeserved credit. Such experiences justify scepticism of the injections and other much vaunted specifics which enjoy ephemeral reputations.

Adolescence, adult and middle life, and early old age, each with appropriate academic and sporting obligations. How much more should I have achieved without this disadvantage? Or is it possible that a certain strength has been derived from a knowledge of my weakness? By that curious law of attraction, I have discovered among my colleagues so many fellow-sufferers as to suppose that duodenal ulcer may displace coronary thrombosis in its claim to recognition as "the doctor's disease."

I have been fortunate in escaping the hæmorrhages that others have suffered, and an X ray, while showing a grossly deformed duodenal cap, clearly proves the absence of stenosis.

So I am encouraged to advance a few generalisations. In diet and in general habits, take reasonable precautions. I wish I could better define what I mean in steering a middle course between "living dangerously" and "safety first." A somewhat fatalistic attitude is desirable. I believe that whether or no bleeding occurs depends on the constitution of the mucosa, so that in some cases no amount of care or precaution will prevent it, whereas in others no extremity of insult or abuse will cause it.

Quite apart from actual ulceration, the duodenum of a susceptible person seems capable of producing pain as a habit—a sort of conditioned reflex. This may be loose thinking; but the mechanism of pain in peptic ulceration is still not completely understood. I believe there really is such a condition as nervous gastralgia, but how could this be distinguished from a so-called "duodenitis"?

For the alleviation of pain I have found the horizontal position, especially on the right side, of distinct benefit though unfortunately impracticable during business hours. I have never received a satisfactory explanation of this effect on mechanical lines. Alkalis have proved disappointing, nor has belladonna helped me. In my stormy days the barbiturates had not yet arrived; regular small doses are probably a good general procedure. Of course I never took opium, and I have not yet encountered a morphine addict who attributed his downfall to the demands of an ulcer.

The so-called hunger-pain appears to be the appeal for gastric distension rather than the indication of a chemical or biological need, if one may judge by the quantity rather than the nature of the ingestion. I regret that I never tried the effect of simple inflation, which would have proved the purely physical element in the relief.

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Nowadays the influence of psychical disturbances in the causation and aggravation of ulcer is universally accepted, sometimes perhaps to an exaggerated extent. It may well be that skilled inquiry could identify the specific emotion that is related to this lesion, as in the case, no doubt, of all psychosomatic disease. Is it dissatisfaction with one's lot or mere boredom? Is it anxiety or fear, and, if so, in relation to what? Is it remorse, sorrow, or domestic infelicity? Is it indignation or the brooding over grievances? Is it vexation at frustration, or disappointment thwarting ambition? Such research might be profitable in individual cases and serve as a guide to the ordering of the patient's life.

In my case, to be called to the telephone in the course of a meal is certain to provoke pain. I have no doubt that on occasion my inquisitor has been annoyed by what he must regard as my disproportionate resentment over an unnecessary disturbance, and has condemned me in his mind as a gormandiser too fond of his dinner to be interested in anything else.

I return to the question-begging "reasonable precautions." The details of diet, alcohol, tobacco, and exercise are individual, and the lesson must be learnt through suffering or the misery of unnecessary self-deprivations; for what in one is a legitimate licence may in another prove to be an undesirable carelessness or over-indulgence.

There are, of course, idiosyncrasies that must be discovered and accepted, but in general I do not believe that drastic food restrictions are necessary or have much to do with relief or cure. Quite early in my career I reflected cynically that the only advantage of the Sippy (or similar) diet was its complexity, which occupied most of the patient's twenty-four hours and by necessarily confining him to bed ensured the really essential element in his treatment. Indeed, as soon as I had charge of hospital beds I treated my ulcer cases with a generous full diet, thus anticipating Meulengracht and others by several years. But I insisted on absolute bed rest. Perhaps recumbency plays a part in the healing process, but I am inclined to think that the advantage is in securing whole-hearted coöperation. Having in this way thrown in his hand, the sufferer's pride is satisfied; the struggle is at an end, and he is shielded from the world's trials and tribulations.

About smoking we shall never attain unanimity. It is in respect to cigarettes rather than tobacco in general that argument continues. In my own case, judging by the experiment of long periods of abstinence, smoking has no influence; and observation of many others has provided no support for an indictment of nicotine or whatever is supposed to be responsible. We shall always be left undecided whether it is that smoking is bad for a duodenal ulcer or that most sufferers are of the type that fly to tobacco for its nervous assuagement. On the whole, I believe there is more disadvantage from discontented deprivation than from indulgence.

Exercise, apart from hygienic considerations, may have some implications. The ambition of the young duodenal subject is as likely to be in the direction of athletic as of academic distinction; and so, as is often the case, cause and effect may be confounded.

During the first world war I sat with Arbuthnot Lane on a medical board which dealt one morning with three consecutive examples in young officers. All three were athletes, two runners and one oarsman. Lane regarded them with great satisfaction as supporting his thesis that peptic ulceration is explicable on anatomical lines. In his view, contraction of powerful abdominal muscles thrusts the viscera down into the pelvis. Traction on the duodeno-jejunal flexure results, leading to duodenal distension with yielding in its first, relatively mobile, part. The era of the psychogenic factor had not yet arrived, but even then I hazarded the suggestion that the highly strung temperament so familiar in athletes might be responsible rather than the physical accompaniments of violent exercise—an opinion which the great surgeon received without enthusiasm.

* * *

Week by week I have read, with admiration and wonder, these descriptions of major disabilities. The courage of those afflicted has been surpassed only by their enterprise and resourcefulness in the determination to lead a useful and enjoyable life. Week by week I have asked myself two questions. Were I in like case, should I have found the necessary strength and displayed such resolution? Compared with these crippling handicaps has not my own been insignificant? I have not been completely hors-de-combat for more than a total of six weeks since my lesion first advertised itself. In the last 28 years, in the hurly-burly of a strenuous professional life that has yielded at least a modicum of success and perhaps even a little distinction, I have not lost one full day's work. According to predilection this might be interpreted as a certificate of stoicism or as evidence of the triviality of the handicap.

And yet, without over-indulgence in self-pity, it may be said that one's enjoyment of life is reduced by an ulcer to a greater extent than by some of the more serious disabilities. Even with the comparative carelessness that I have advocated, one is compelled to live the life of a physiological prig, ever thoughtful of the danger of taking liberties, shrinking from enterprises and undertakings which would necessarily entail alimentary or dietetic trials and risks.

The chronic dyspeptic, when brooding over his lot, reflects that the blind, the deaf, or the maimed may by their adjustments be rendered happy and contented; that the diabetic's well-being can be mathematically regulated; and that even the subject of heart disease may carry on cheerfully though limited in one particular sphere. But the sufferer from duodenal ulcer is characteristically of the type that will not compromise. He refuses to come to terms with himself, let alone with the world. Unless some catastrophe such as hæmorrhage or perforation makes surrender incontestable, he will persist in the thick of the fight, even with one arm perpetually tied behind his back. As George Meredith says of Hippias Feveril, one is not altogether fit for the battle of life who is engaged in a perpetual contention with his dinner.

Public Health

Influenza

Deaths in the great towns of England and Wales.—In the week ended Jan. 29 there were 37 deaths against 45 in the preceding week. In the first four weeks of 1949 the deaths were on the whole fewer than in any previous year except 1948.

Incidence.—There have been several reports of scattered outbreaks of apparently true influenza in camps and residential schools, and virus has been isolated from some cases. Generally speaking the disease appears to be mild with fever lasting about 4 days.

Virology.—The current English strain has not yet been finally identified, but one French and two Dutch strains seem to be identical serologically and related to, though not identical with, the English 1947A strain (F.M.1 of the American workers). All these strains are quite remotely related to the P.R.8 strain of virus A.

Spread in Europe.—It now appears that influenza was present in some parts of Italy and its islands in October and November, 1948. By Jan. 31, according to the W.H.O., the infection had reached epidemic prevalence in France, Belgium, Southern Netherlands, and four frontier cantons of Switzerland; there was considerable incidence in Bulgaria, Slovakia, and the Austrian Tyrol; and there were foyers of infection in Finland (Helsinki), Turkey, and the French zone of Germany. No abnormal incidence was reported from Denmark, Norway, Sweden, the United Kingdom, Ireland, and Spain.

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In England Now

A Running Commentary by Peripatetic Correspondents

BETWEEN us, my husband and I have 4000-odd souls under our care; and at moments when none of them needs anything whatever in the way of attention, advice, or reassurance, our telephone is silent. But February is not a very good month. On a Monday, seventeen calls per breakfast are quite usual, and one needs rather more vitality and sang-froid than I command on any morning in order to integrate them successfully with family life.

It is rather difficult to avoid blaming the N.H.S. for the present unequal struggle; but one ought to try to disentangle this new factor from the others which always have combined to make the winter a difficult time for the G.P.'s family.

For instance, the fact that our family and patients are now right on top of each other is due as much to the growth of the family and to the war (preventing the planned additions to the house) as it is to seasonal incidence of illness and to the patients' determination to by-pass the new regulations via the telephone. Too bad that all this should happen just when domestic help is so scarce and precarious, when housekeeping is at its most difficult, and when the children's developing personalities clamour for outlets, for Lebensraum, and for individual attention of every kind. But there it is; and the N.H.S. provides the perfect scapegoat for all the ills which have accumulated through years of mismanagement aided by misfortune.

Some ten years ago our professional resources could only just be exploited by a full recruitment of such private resources as a doctor's house can muster; since then the professional resources have gone up by leaps and bounds, making it easier and easier to tackle more and more work, while the private resources have dwindled to almost nothing. With a lot of grumbling we were somehow keeping the dual concern together in one piece, when in stepped the new administration with a bold programme which ignores both the need for "domestic" resources and their total absence. In so far as the health centres are too remote and nebulous to enter into any constructive planning for the immediate future, the N.H.S. has delivered what feels like a final blow to the rickety structure which it was intended to strengthen.

This blow is generally represented as a threat to medicine, which it is feared may become shoddy as a result of the provisions of the new service. It happens to be the only fear I do not share. The doctor alone can make medicine shoddy, and it takes a special person to make that kind of doctor; he must have succumbed to the temptation long before July 5. My worry is rather lest the man who is incapable of shoddy medicine may find it impossible to flourish—personally—in general practice.

Student selection is likely to give us able recruits and it is hardly to be feared that these will be led astray by purely professional considerations; but it is very much to be feared that they will not be attracted by general practice if they know in advance what kind of limitations it imposes on a man's unprofessional life. The successful G.P. is par excellence the doctor who has made good as a man, a husband, and a father. It is very much within his province to help his patients make good in all these respects, and one does not embark upon such a mission out of a vacuum: one depends indeed on a background rich both in experience of life and in inspiration to unremitting effort. Where but in his own home should a doctor look for these, and why should anyone find it easier than John and I do to have a home life at all, let alone a stable and vigorous one?

Our practice has spread—if I may put it so—from the consulting-room to the drawing-room and even to the front door; advice is sought along any and every channel which promises to obviate a long wait in the surgery, and it has made privacy in our home a much-lamented luxury of the past. Before blaming the patients it is as well to remember that, in deciding whether they are "able" to attend surgery, they are asked to decide whether a child, say, with a cough is fit to join a bus queue on a raw February night, fit to wait in a crowded surgery, and fit to face whatever the return journey, broken by a visit to the chemist, may have in store. Who would *not* try to find a short cut, if one existed, and who would trouble to examine the consequences to the doctor's family if this short cut were resorted to habitually? Yet it is the consequences to the doctor's family which will eventually deprive the patients of their doctor; or at least, of the services of such men as are most eager and best able to help them.

It is the "house built on rock" which is the general practitioner's fund of vital energy and serenity. His day's work is played against a rich kaleidoscope of human situations—tragic, joyous, bewildered, troubled; each calls for some special gift or skill of his, but all, without exception, depend on the same invulnerable core of serenity without which he could not be a good doctor. Patients must never have occasion to fear that the doctor may be nervy, or anxious, or depressed when called upon to help; to appeal to such a man would be to add his troubles to one's own, not to transfer them to broader shoulders. But broad shoulders have their own demands; one cannot see them on a man who himself lives in a strained atmosphere, who comes home to find a rebellious family or an ever-weary wife. If he is helpless to mend matters in his own home, he will, in time, cease to be the ray of sunshine his patients so confidently expect.

Years ago, when home and practice were distinct, there was some point in coming home if one wanted play instead of work, or wanted to get away from worries instead of looking for fresh ones. (I do not mean a fresh lot of calls—these were always to be had—but fresh evidence that the household was cracking under the strain of the new calls.) Today, the work itself is more congenial than ever before, and if John wants rest and recreation he goes out and does a round. But what if he feels like coming home for lunch, and what of the children, who are unanimous in declaring that it is "beastly unfair" to have a doctor for a father? I suppose that for every message which the servant used to take at the patients' door I now take some ten telephone calls myself. Like the family, these tend to congregate at meal-times, and you may imagine what this means in terms of domestic privacy—to say nothing of the reception which awaits the caller who has the misfortune to be tenth. He, poor devil, imagines that he is saving himself and the doctor trouble by trying for a quiet chat when the doctor is most likely to be in for lunch; it does not occur to him that another dozen of his fellows may have been vouchsafed a similar inspiration, and that the doctor is best advised not to come home if it is either lunch or quiet that he wants.

This of course is not a sudden development; we've been asking for it by allowing the practice to grow regardless of the strict limitations of the household—the soil on which it is ordained that a medical practice must grow. But you can see how the changes incumbent on July 5 have come to make just that difference which counts. For one thing, expansion rather than limitation is the order of the day; for another, no matter what one says or does, the patients remain convinced that their insurance stamps pay for their medical attendance, and they *will* have their pound of flesh. Many of them really want help and genuinely want to save us trouble; but they simply have not the imagination to realise what things may be like at the other end of the wire.

The other day a young friend who is about to qualify came to ask for advice and information as to his probable fate in general practice. He is gifted enough to tackle anything, and I was a little startled to hear John say: "I cannot really advise you; whether or not you will flourish in general practice depends largely on the personality of your future wife and on your programme in the matter of begetting and rearing children. In London you might reckon to be free to lead the life you want and to have a flourishing practice as well in three years' time." This is a frank acknowledgment of the open clash between social and professional aims; it happens to be important in general practice because the person who is best suited to make a good job of it is also the person who is naturally sociable and least inclined to neglect his home life or his obligations as a father and husband. Would you say that the health centres are likely to arrive in time to prevent the discouragement of the most nearly fit to be our good G.P.'s of the future?

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If one could lay down any precept at all for the general practitioner, it would sound something like "Live well and wisely yourself, so that you may teach your patients to do likewise"—though one must first love them enough to bother with any teaching. But who can live wisely in a home which is the scene of perpetual noise and commotion? And how is one to learn to love the perpetrators of chaos in one's private sanctum?

* * *

It's a bit hard to wake in the morning and find you have been living in a district of highly doubtful morality. If you read the *Pictorial* the other Sunday—and about three million people did—you will know that dear old Chelsea is the centre of vicious practices surpassing in voluptuousness and ingenuity those of ancient Babylon, pre-war Marseilles, and Hollywood in the 1920's. The residents of S.W.3, according to the paper, need only a little encouragement to indulge in assorted aberrations, with a violently masochistic and sadistic background, though there are hints of even more immoral goings-on, of which drug-addiction (non-specific) is the most wholesome. The sites of these orgies are, naturally, "studios," proving that the British Public has not changed its conception of the artistic life since the middle of last century.

We in Chelsea don't really mind if the papers say that past South Ken tube-station all moral standards drop to the ground and that the 22 bus route passes through hell; that naked women dance nightly in Cheyne Walk in memory of that old voluptuary Carlyle; that ribald laughter floats after dark from the windows of the Lister Institute; that there are rumours of wild debauches in the Royal Hospital; and that no decent housewife dare linger in a fish queue on the King's Road. But one thing we cannot stomach: we will not be referred to as a *suburb*.

* * *

As a successful candidate in the recent contest with the Censors, I must own to having had an unfair advantage over some of my competitors. Readers of this column, even if they did not sit the Membership this time, will have gathered that there was a question about an 18-months-old child. Our small son reached that age almost on the very day I sat for the papers. A short pen sketch and, hey presto!—the answer was written. But I confess I did him more than justice. I made him a sturdy toddler, when in truth he doesn't even walk, for his ataxic stagger from chair to chair, punctuated by episodes of industrious crawling, can scarcely be called that. And the things I did want to talk about, such as his preoccupation with screw-on lids and his habit of removing the silver from the sideboard and tucking it in the recesses of the armchairs, seemed outside the scope of the question.

The moral? Get married and raise a family. One damp napkin that you have changed yourself is worth several lectures on child management. Furthermore, you bachelors will find that the extra responsibilities are very helpful in keeping your nose to the grindstone.

* * *

We had a nice view of the sun-spots this week on my bedroom wall. When I was a boy there was an eclipse of the sun, and I noticed that all the vaguely circular mottled shadows on the ground under the rose-arch became startlingly crescentic. When I looked out of my window on Sunday morning and saw my family fumbling with smoked glass I recalled this ancient experience. Fortunately the sun shining through the ivy round the window was throwing suitable shadows over my bed. So it was easy to find a clear circle at the edge of the mottlings, catch it on a sheet of white paper to make it clearer still, and then yell triumphantly for my sons to see the two fine macules.

* * *

How careful one has to be in any reference to the young nations! There was an indignant scene at a D.C.H. course last year when an innocent lecturer asked an Asiatic student if hæmophilia occurred in her country. "We have every disease in Xyz," she replied.

Letters to the Editor

ANTICOAGULANTS IN CORONARY THROMBOSIS

SIR,—In your leading article of Jan. 29 you submit a convincing case for the use of anticoagulants in the treatment of coronary thrombosis, based on empirical evidence. I would suggest that the justification for this treatment is now established on a scientific basis.

For many years clinicians and pathologists have felt compelled to conclude that of the two factors concerned in the production of coronary thrombosis—the local disease in the artery and a clotting tendency in the blood—the latter is, sometimes at least, the more important. Bourne [1] pointed out in 1934 that the majority of people with atheromatous coronary arteries die without coronary thrombosis, and it might also be said that some people who die from coronary thrombosis have little coronary atheroma. It must be a common experience to find that the coronary event is but one incident in a widespread thrombotic condition. Bourne cites 5 case-records in which the coronary lesion was coincident with thromboses in other arteries and in veins; and in a review of post-mortem findings in coronary thrombosis Meakins and Eakin [2] noted the existence of thrombosis in other systems, arterial and venous, in all but 4 of 62 cases; they concluded that in this affection there must be some general tendency to thrombosis. It is scarcely necessary to labour this point; personal experience and the literature on the subject can supply abundant evidence to justify the conclusion that this clotting tendency is of primary importance.

With this in mind the recent work of Duguid [3] and of Harrison [4] assumes great significance. In his original article Duguid claims to have shown that the lesions we classify as atherosclerosis may arise by organisation of a mural thrombus. His photomicrographs show all stages of this process from wisps of fibrin clinging to the arterial wall to massive deposits with atheromatous softening. In a later article he shows that a similar process is of common occurrence in the aorta. He supposes that in the superficial streaking and in the cholesterol sclerosis of rabbits the lipoid deposition is presumbly the result of disordered fat metabolism, and that this change in the arterial wall may determine the site of fibrin encrustation, but the implication is that atherosclerosis depends not only on factors which act upon the tissues of the vessel wall but also on those that govern fibrin formation in the circulating blood. Harrison, approaching the subject more directly, succeeded in producing in the pulmonary arteries of rabbits lesions morphologically indistinguishable from arteriosclerosis, by injecting finely fragmented fibrin clot into their ear veins.

I would submit that it is reasonable to conclude from all this evidence not only that a clotting tendency is an essential feature in the pathogenesis of coronary thrombosis, but also that the lesion in the affected artery, which determines the locality of the thrombosis, may itself be caused by this same clotting tendency. In other words, that an increased coagulability of the blood is the beginning and the end of the process that results in coronary thrombosis. It is for biochemists to discover the origin of this disorder; we know that the liver produces fibrinogen and prothrombin, and probably heparin too, and this may point the way to further research; but, however this may be, until we can track the fault to its ultimate source and can apply effective remedies there, we must do all that we safely can to reduce the coagulability of the blood, and if possible maintain this reduction until the clotting phase passes. How this can best be done is another question that will be dealt with later; but meanwhile we should surely accept in principle the idea that the use of anticoagulants is an essential part of the treatment of coronary thrombosis.

Torquay. PAUL GIBSON.

1. Bourne, G. *St. Bart's Hosp. J.* January, 1935, p. 81.
2. Meakins, J. C., Eakin, W. W. *Canad. med. Ass. J.* 1932, **26**, 18.
3. Duguid, J. B. *J. Path. Bact.* 1946, **58**, 207; *Ibid*, 1948, **60**, 57.
4. Harrison, C. V. *Ibid*, p. 289.

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THE WRONG DRUG

SIR,—The drugs having names ending in "—caine" have been so named deliberately to draw attention to their local anæsthetic properties. Far from being a cause of confusion, this suffix should warn users that they are handling a dangerous substance. If the names were changed to something more closely indicating chemical structure, confusion would be even worse.

It cannot too strongly be impressed upon all who handle drugs that every one of them is a potential poison. Even distilled water can be dangerous if incorrectly used. Nothing can take the place of constant vigilance and accurate reading of labels. Accidents such as those noted in your annotation of Feb. 5 will continue until nurses, anæsthetists, and surgeons learn the necessity of reading the label and checking the dose of every drug they handle. Considerable care is exercised by the surgeon in checking over the instruments he is going to use, and by the sister in counting swabs. These materials are all double checked as a routine. But when it comes to drugs too much is taken on trust. An unlabelled ampoule is offered to the anæsthetist, or the label of a bottle has become illegible and has not been returned to the pharmacist for replacement.

I would suggest that the hospital pharmacist is the officer who can do most to assist in educating the staff in these matters, and he should insist on written orders for all drugs and should take the necessary action to see that labelling is clear and unequivocal. If the name of the drug appears clearly on the container I can see no reason why it should not be carefully read. The great danger of coloured solutions is that the users come to depend on the colour instead of the label, with the result indicated in your note on the red colouration of cocaine.

Whilst it may be desirable for a theatre sister to know the relative toxicities of the local anæsthetics, it is by no means necessary. It is desperately necessary that she should be able to read accurately, and the user, anæsthetist, or surgeon should read the label as a check. There is no easy short cut. Clear labelling and accurate reading provide the answer.

Westminster Hospital, London, S.W.1. HERBERT S. GRAINGER.

SALARIES AND STATUS OF MEDICAL RESEARCH-WORKERS

SIR,—We welcome the initiative shown by the Association of Scientific Workers in drawing up a memorandum on the salary of the research-worker (Jan. 22, p. 154). We agree that the discrepancies between the rates of pay of research-workers and clinical specialists is not only unjust to the former but also makes recruiting of research-workers difficult. The threat of a drift of those already in research to more remunerative clinical appointments is real and must be avoided if we are to maintain and advance our international position in medicine.

While we welcome the recommendation to increase the salaries of research-workers, we disagree that a research-worker of any grade should have to accept a salary less than his colleagues in the clinical specialties, whether the difference is 10%, 20%, or any other figure. Such a proposal is tantamount to admitting that research is so much less important to society than clinical practice. In the past two main arguments have been used to limit the salaries of research-workers. The first is that research is a vocation; and the second that research-workers miss the "hurly-burly" of clinical work. In our opinion these arguments are fallacious. If research-workers were paid equally with other specialists, there would be no economic limitation to the attraction of the best men into research. Furthermore, many research-workers do not live in "ivory towers"; most of them have as active a life as clinicians, and many of them have a certain degree of clinical responsibility.

We consider that some of the recommendations for the grading of workers in research may give rise to anomalies. Nobody entering upon a research career should have to lose financially, and the salary of the research trainee should be adjusted to take this into account. On completion of a preliminary training-period of twelve months or so, he should be graded as a specialist registrar and be paid the corresponding salary. If the research-worker is considered capable of continuing his work after a period of three to four years he should be accorded specialist status.

We should like to emphasise the necessity of according full specialist status to research-workers at that stage in their career when, had they been engaged in purely clinical work, they would be regarded as specialists—i.e., about the age of 32, as mentioned in the Spens report. We wish to avoid the injustice of grossly underpaid research-workers of considerable experience. The principle of equality of pay would allow easy transfer of a clinical specialist to full research work in his own specialty, and make use of the research capacity of a large number of clinical specialists.

The association's recommendation that *administrative* responsibility should be considered in the grading of those at present engaged in research is unwise and may encourage too close a parallel with the Civil Service system. The value of administrative *ability* is not denied, and where a research-worker's duties involve additional work of administration and organisation—e.g., as director of a department—he should receive additional remuneration. We agree with the memorandum that medical research-workers who are not medically qualified should be paid on the same scale as the medically qualified.

We should welcome the opinions of other research-workers on this issue.

BIRMINGHAM RESEARCH-WORKERS.

WEATHER AND ILLNESS

SIR,—It appears that the influence of weather on cerebral conditions [1] and on rheumatism [2] may be similar to its influence on allergy.

In the years 1936–39 complete records were obtained of attacks of asthma, urticaria, angioneurotic œdema, and migraine experienced by over 300 patients who attended our clinics every week. This group of patients did not include any who were having frequent attacks, and those attacks of patients included in the group which could actually be accounted for by respiratory infections and obvious psychological causes were also discarded. Analysis of the remaining 1700 attacks indicated that the number of bad days (days when the number of attacks experienced by the group was large) was appreciably larger than would be expected by chance.

Attempts were made to correlate these bad days with single meteorological phenomena, but they were unsuccessful. It appears likely that the external trauma concerned is rapid rise or fall in cooling power; the greater the rate of change of cooling power, the more marked are each patient's symptoms and the greater the number of patients affected. Attempts are now being made to correlate the data with meteorological observations on this basis.

Department of Allergy, Wright-Fleming Institute of Microbiology, St. Mary's Hospital. W. HOWARD HUGHES.

Department of Physics, St. Mary's Hospital Medical School, London, W.2. D. A. TANFIELD.

OXYGEN THERAPY IN SHOCK

SIR,—May I support Dr. Ohlsson's plea (Jan. 15) for more intensive oxygen therapy in wound shock? The rationale of this is so logical that I am always surprised at the sceptical attitude of many surgeons.

As Dr. Ohlsson says, oxygen therapy may just turn the scale to break the vicious circle initiated by shock. Clinically I am strongly influenced to believe that this is the case, and in your columns had occasion to stress this belief with regard to air-raid casualties.[3] Admittedly some patients with wound shock do not improve with oxygen therapy, but I believe that it may be life-saving in others.

During and since the war I have been greatly struck, in more than one hospital, by the carelessness with which oxygen therapy is administered. Despite all the teaching of the last few years one still sees oxygen given by the funnel method or by nasal catheters. If the B.L.B.

1. Annotation, *Lancet*, Jan. 1, p. 30.
2. Whiten, A. J. *Ibid*, Jan. 8, p. 81.
3. *Lancet*, 1941, ii, 785.

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mask or some similar device is used, one usually finds that it is fitted badly and regulated wrongly. Better results would be obtained with oxygen therapy if surgeons would devote some time to the tuition of their housemen and nursing-staff in the correct usage of the B.L.B. mask. Incidentally, I consider that this mask is far superior to more modern 'Cellophane' flimsy structures which, as often as not, are found over the patient's eyes or around his neck rather than over the respiratory orifices.

Liverpool. JOHN A. SHEPHERD.

HISTOPLASMOSIS AND PULMONARY TUBERCULOSIS

SIR,—Your leading article last week suggests that no infection with histoplasma has been demonstrated on this side of the Atlantic, and that small investigations in Holland and in Eire for histoplasmin sensitivity were negative.

I believe that Dr. J. T. Duncan, of the London School of Hygiene and Tropical Medicine, diagnosed 2 cases in England, in both of which the patient had earlier travelled in Africa or Asia. I should also like to draw your attention to a survey of university students in Cardiff which I made,[1] and which is apparently the only series reported from Great Britain. This study yielded negative results for histoplasmin sensitivity in students with pulmonary calcification.

Cardiff. BRIAN H. MCCRACKEN.

FELLOWSHIP FOR FREEDOM IN MEDICINE

SIR,—In December last you published a letter from us inviting medical men and women to join the fellowship. Would you be good enough to state that we have now established our permanent offices at 45, Nottingham Place, London, W.1?

G. H. ROSSDALE
E. C. WARNER
Hon. Secretaries, Fellowship for Freedom in Medicine.

LIVER EXTRACTS

SIR,—I read Dr. McSorley's letter of Jan. 22 with great interest. The problems he raises have been concerning me for some time. I have found the same disproportion between the doses recommended and the actual amounts required by patients with pernicious anæmia; and in the case reported (Dec. 11) relatively small doses were given intentionally for a time.

Many manufacturers appear to work on the principle that if, as the result of an injection of liver extract in a typical case of pernicious anæmia in severe relapse, the reticulocyte response and/or the rise of red blood-cells for 14 days conform to the criteria of adequacy suggested by the work of Minot et al.,[2] Isaacs et al.,[3] and Della Vida and Dyke,[4] this dose will, if repeated at the same interval, bring the red-cell counts to normal in the majority of cases. Many manufacturers, while not stipulating the actual duration of initial therapy, do advise that it be continued until the blood-count is normal. This period is of course rarely less than 3 months even with adequate doses.

In my experience, however, it is exceptional, with the extracts available in this country at present, to observe the optimal rate of rise of red cells continue for 14 days after a single injection of liver extract in the amount recommended by the manufacturers, or for the bone-marrow to be completely normoblastic at the end of this time. Usually at the end of 10 days or less the count has levelled and started to fall, and the bone-marrow is becoming megaloblastic again. With these extracts given in the recommended doses, normal counts never seem to be obtained, and the patients reach equilibrium between 3,500,000 and 4,500,000 cells per c.mm. With extracts that do really fulfil the claims made for them, and which do produce a completely normoblastic marrow, a steady progression to normal counts is usually seen. In these patients it may be possible later to increase the intervals between the injections and still maintain the counts at normal levels. An example may help to underline these points.

The red-cell count of a patient with pernicious anæmia treated for almost a year in 1946–47 with 2 ml. a fortnight of a concentrated British extract, failed to rise above 4,000,000 per c.mm. The patient then neglected to attend for treatment, and her condition relapsed. Later she was given a concentrated American extract in the same dosage as before. Her count rose to normal values within 3 months.

I certainly do not consider doses of this order satisfactory in ordinary practice. As Dr. McSorley says, this is a minimal dosage. Even with fully potent extracts it will only be satisfactory in a proportion of cases; many will need considerably more. But not only should the dosage schedules be revised; the potency of extracts should be more critically assessed.

Department of Pathology, Postgraduate Medical School of London. D. L. MOLLIN.

THE HOSPITAL ADMINISTRATOR TODAY

SIR,—Admirable as the article in your issue of Jan. 29 may be, I suggest that one at least of its warnings is very urgent and deserves much more emphasis. The danger of submergence in office routine and committee work is great, and indeed threatens all members of staff who are involved in the volume of discussion in the new service. Associated with this is the menace of excessive lay administrative staffs, which in some areas are greater than those of regional boards; this is more serious because officialdom is the enemy of good individual care of the sick. Indeed evidence is accumulating that some are exploiting hospitals merely as means of providing lay careers. Among many difficulties of the administrator not mentioned is the tendency to pay the group secretariat at higher rates than the clinical secretariat, following an official directive, and at higher rates than experienced members of other grades from assistant pharmacists to engineers.

There is, then, the understandable but inexcusable omission of anything more than passing mention of the medical administrator. In point of fact, as probably most of your readers know, it is very exceptional for any hospital in Scotland not to have a medical superintendent, and in England and Wales it was only those hospitals which needed constantly to appeal for voluntary support which needed special officers to organise appeals and to manage their business affairs. Amongst this limited number of men there have been not a few who have so identified themselves with the hospitals whose funds were their concern that they brought honour both to their hospitals and to themselves. But they remained the exceptions, and even so there were usually senior members of the consulting staff who unofficially exercised extensive authority in what may be called medical administration. Though it might be invidious to quote names, surely Lord Moran at St. Mary's, Lord Webb-Johnson at the Middlesex, and Mr. Philip Mitchiner at St. Thomas's have been so outstanding as to be quoted without offence. In the more numerous group of hospitals maintained at public expense, including those for mental, infectious, and tuberculous conditions, as well as those for general diseases, the principal officer was invariably a medical man, usually practising a specialty in addition to exercising general supervision in the interest of the medical care of the patients. After all it is the patients, and not the administrative or other staff for whom the hospitals exist, and that is a basic principle which needs special emphasis now that signs of subordinating it to bureaucratic dominance are appearing in many insidious ways. The cleanliness, warmth, cooking, laundry, general atmosphere, and arrangement—all should be directed to the well-being of the sick, which implies constant responsiveness to medical (and nursing) considerations. Though it is true that these professional views are the concern of the medical committee, for day-to-day purposes there must be one member of the senior professional staff in whom they are centred, no matter what office he holds or by what name he is called, of such experience, standing, and personality as to accept responsibility for his own and others' mistakes. Just at present, for example, one of the most serious and distasteful decisions, constantly

1. *Thorax*, 1948, **3**, 45.
2. Minot, G. R., Cohn, E. J., Murphy, W. P., Lawson, H. A. *Amer. J. med. Sci.* 1928, **175**, 599.
3. Isaacs, R., Bethell, F. H., Riddle, M. C., Friedman, A. *J. Amer. med. Ass.* 1938, **111**, 2291.
4. Della Vida, B. L., Dyke, S. C. *Lancet*, 1942, ii, 275.

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called for, is the choice of applicants to be admitted to the relatively few available beds, and reference in case of need to some final authority is essential.

The article ended with a quotation which pointed to the danger confronting us all today—namely, that hospital work may be divorced from the needs of the community. In this context those needs are medical needs, and no vested interest or preconceived idea should be allowed to blind us to the danger of subordinating them to a bureaucratic ideal. For a hospital to be effective in meeting those needs and efficient in its maintenance adequate professional, nursing, and business managements are essential. All must coöperate to the highest degree, but none can take precedence over the professional.

St. Stephen's Hospital, London, S.W.10. R. KELSON FORD.

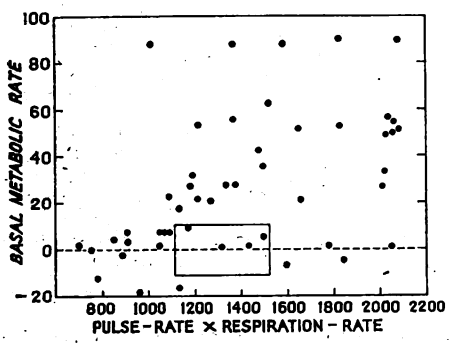
SPLINTAGE FOR HAND SURGERY

SIR,—I have read with interest Mr. Fisk's description (Dec. 25) of his splint for hand surgery. I have used the splint for some time and cannot speak too highly of its usefulness. The hand is difficult to control on the operating-table, and frequently an extra assistant is needed simply for this purpose. The lead splint performs this function admirably and has become an indispensable part of my equipment. Mr. Fisk is to be congratulated on designing a simple and efficient instrument.

Derby. R. GUY PULVERTAFT.

ESTIMATION OF BASAL METABOLIC RATE

SIR,—In the chemical pathology department of St. George's Hospital we have for some years used the Benedict-Roth method for measuring basal metabolic rate. We believe that this method is used in many laboratories throughout the country. Dr. Bene's article, published in your issue of Jan. 22, was therefore of considerable interest to us. We have plotted here 50 unselected cases from our records, graphing the "R.P. index" according to Dr. Bene against the basal metabolic rate estimated by the Benedict method. On the graph the frame encloses the normal range for R.P. index as outlined by Dr. Bene and the normal range obtained by the Benedict technique. We follow Boothby and Sandiford in taking ±10 as the normal limits.



It is clear that if a reasonable relationship exists between the two methods, the majority of normals should fall within the frame. They did not. Dr. Bene claims, moreover, that an R.P. index above 1500 indicates a raised basal metabolic rate. Again the graph shows a striking discrepancy.

It would seem that whatever the R.P. index measures, it does not tally with the basal metabolic rate as measured by such a well-established technique as that laid down by Benedict and Roth.

St. George's Hospital Medical School, London, S.W.1 J. J. LOVELL
N. H. MARTIN.

OBJECTS OF RESEARCH

SIR,—Professor Alstead (Jan. 29) warns us against the present dangerous trends towards ultra-specialisation. It is true that specialisation has permitted great developments in certain branches, and the physician should have specialised leanings; but it would certainly be a mistake, as he says, if geriatrics were to become departmentalised, as is now threatened. His contention that the ordinary care of the aged comes within the province of the general practitioner and general consultant should be wholeheartedly endorsed, for the sake of physician, patient, and medical education alike. Least of all patients can the aged be labelled like laboratory specimens, and their problems recur each day in the general practice of medicine. To create a specialty of geriatrics might well give the signal for yet other artificial subdivisions, and would throw to the wind Walshe's contention that the "specialist must cling fast to the foundations of medicine for only thus can he integrate his contributions to medicine and orient them."

London, W.1. PHILIP ELLMAN.

SENIORS AND JUNIORS

SIR,—Your correspondent of Jan. 29 is evidently blissfully unaware of the intentions of the Ministry with regard to senior and junior consultant staff. The assessing committees appointed to advise the regional hospital boards on the status of their consultant staffs are instructed to cut down the present quota of consultants by relegating the more junior ones to a nebulous category of "senior hospital officers"—thereby achieving economy in one direction, since this category will be paid at a lower rate than full consultants. As Spens recommends appointment to full consultant status at the age of 32, the present junior full consultants with higher degrees will presumably have to be lowered in status (to senior hospital officers) on the sole remaining ground of insufficient experience, wherever this can be fairly (?) justified.

Further economy will be practised on those senior consultants who have escaped the former type of axe, by cutting down the number of sessions at present allocated to part-timers.

PHYSICIAN.

Medicine and the Law

After-effects of Intravenous Anæsthesia

A CASE which was successfully taken up by the Medical Protection Society exemplifies the need for close supervision of patients recovering from anæsthesia by a barbiturate injected intravenously.

A dental surgeon intended to extract seven teeth in a patient for whom nitrous oxide was deemed unsuitable. The patient was told that he was to be given an intravenous anæsthetic and that he would "probably be very drowsy for at least an hour after the extractions." The patient's own doctor injected 5·5 ml. (0·55 g.) of soluble hexobarbitone; the teeth were extracted, and the patient was carried to a couch in the surgery. Niketharnide was injected to accelerate recovery.

About a quarter of an hour later the dental surgeon went to lunch, instructing the nurse to report to him if the patient began to come round. Within a few minutes the nurse reported that the patient was fingering his shirt at the neck. Returning immediately, the dental surgeon found the patient apparently asleep; so he returned to lunch.

Twenty minutes later the nurse, who had kept looking into the surgery, found that the patient had gone. It transpired that he had driven off in his car, and that, when stopped by traffic lights, had been addressed by a policeman who, suspecting that something was amiss, kept him in conversation. The constable learned that the patient had just had teeth extracted; he offered to drive the patient home, but the offer was refused. On reaching his garage, about a mile farther on, the patient collided with a wall and a petrol pump, and on getting out of the car he collapsed and was helped upstairs; he remained semiconscious for a further 4–5 hours.

The dental surgeon's claim for the amount of his fee was met by a counter claim for damage to the car, arising through negligence in that, inter alia, the nurse had not prevented the patient from leaving the surgery while still under the influence of the drug. The patient also claimed damages for having been stopped by a police-constable.

The county-court judge who heard the case ruled that the dental surgeon and his nurse had given all the attention the circumstances seemed to require. The patient had been warned of possible after-effects, and

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he had made an error of judgment in going by car to the operation without arranging for someone else to drive him home. Moreover, on the way home the patient had so far recovered as to be capable of making a sound independent judgment of his movements and of whether he should accept the constable's offer to drive him home. His decision to drive himself home without the dentist's permission constituted a *novus actus interveniens*, which broke the chain of causation of the damage. Judgment was given for the dental surgeon for the amount of his fee with costs; and the counter claim was dismissed with costs.

Experts who gave evidence expressed the opinion that the process of recovery from intravenous barbiturates is not always predictable, and that patients receiving them should be escorted home.

Parliament

QUESTION TIME

Industrial Disease in North Staffs

Dr. BARNETT STROSS asked the Minister of National Insurance how many men in the North Staffs coalfield had been examined since July 5, 1948, by the Silicosis Medical Board; and in how many cases had the men been advised that they were suffering from pneumoconiosis or silicosis or silico-tuberculosis, and how many of these had been further advised that they might continue their former work or alternative work, and in what instances had this advice been accepted.—Mr. TOM STEELE replied: During the period from July 5, 1948, to Dec. 31, 1948, 28 miners employed in North Staffs were examined by the Pneumoconiosis Medical Board under the Industrial Injuries Act, and 23 were found to be suffering from pneumoconiosis. Of these, 9 were advised that they could continue in the coal-mining industry under approved conditions and 5 said they proposed to do so. During the same period, 35 men were examined in connexion with claims under the Workmen's Compensation Acts. Of these, 15 were found to be suffering from the disease to a dangerous degree and were suspended. Dr. STROSS: Is it an accepted principle that in all cases where men are advised that they may return to work they will be protected from excessive dust in the mine in which they worked which contributed to or caused the original pneumoconiosis?—Mr. STEELE: The medical board advise these people that they can return to work under approved conditions, and we are in consultation with the National Coal Board and its mine inspectors to ensure that these improved conditions will be maintained.

Dr. STROSS further asked the Minister how many men and women had been examined by the Silicosis Medical Board since July 5, 1948, in the pottery industry in North Staffs.—Mr. STEELE replied: During the period from July 5 to Dec. 31, 1948, 489 persons employed in the pottery industry in North Staffs were examined, either on a claim to benefit or on an initial or periodical examination, by the Pneumoconiosis Medical Board, of whom 40 were found to be suffering from pneumoconiosis. None of them were advised to return to their former work; but 9 of them being skilled men have said they intend to do so. Dr. STROSS: Is it intended to see that the men have some protection after return to work, particularly in view of the fact that silicosis among potters can advance very rapidly, even when such protection is given, and obviously very much more actively when they are not so protected?—Mr. STEELE: None of the men who are suffering from pneumoconiosis is advised to return to work. It lies with the medical board whether or not to suspend the men. There are no similar conditions in pottery as in mining, for which we have approved conditions.

Mr. A. EDWARD DAVIES: If it is impossible for potters and some miners to return to their former occupations can they be provided with alternative employment?—Mr. STEELE: That is very much in the mind of the Minister of Labour who is concerned with that aspect of the problem.

Too Many Patients

Mr. MARTIN LINDSAY asked the Minister of Health how many people had received EC/Reg.107, dated Jan. 14, from the National Health Service Birmingham executive council, informing them that they must change their doctor.—Mr. A. BEVAN replied: The executive council's letter of Jan. 14 was sent to 3196 people. They were all on the list of a single-handed doctor whose total list amounted to 8279, or over double the number agreed with the medical profession as the maximum which can be properly attended by one doctor. The action was taken in consultation with the doctor concerned and I see no reason to question the executive council's action.

Cost of Refresher Courses

Mr. HUGH LINSTEAD asked how much public money had been paid out in respect of refresher courses under clause 48 of the National Health Service Act at the last convenient date.—Mr. BEVAN replied: During the period July 5, 1948, to Jan. 31, 1949, payments in respect of refresher courses under section 48 amounted to £1335. In the same period payments amounting to £1982 were made in respect of refresher courses for ex-Service doctors and dentists. There are in addition a large number of residential and other appointments in hospital for ex-Service doctors.

Treating the Visitors

Colonel M. STODDART-SCOTT asked the Minister if any payments had yet been made to the doctors in the National Health Service for the treatment of temporary residents, visitors, holiday-makers, foreigners, and those patients not on a doctor's list: upon what principle payments were made; and how much was still owed to the doctors for this service.—Mr. BEVAN replied: No payments have yet been made for the treatment of temporary residents, visitors, holiday-makers and foreigners. The principles on which such payments shall be made are still under discussion with the medical profession. It is contemplated that payments in respect of the period from July 5, 1948, to Dec. 31, 1948, will be made at March 31. The amount of these payments is not yet known.

Sir HUGH LUCAS-TOOTH asked the Minister which other countries afforded the benefit of a health service to British visitors.—Mr. BEVAN replied: So far as I know this country is the only one that provides such a service for its visitors at present.

Pay-beds

Mr. E. H. KEELING asked the Minister whether a patient occupying a bed in a pay-ward was required to undertake, in advance, to vacate the bed if it was needed for an urgent case; and if, in that event, any refund was payable.—Mr. BEVAN replied: I have given no instructions to hospitals to require an undertaking of this kind. If a patient occupying a private pay-bed under section 5 of the Act agrees to be moved into a general ward bed in order to make room for another patient who requires privacy on medical grounds he will, of course, pay no charges in respect of the remainder of his stay in the hospital.

Shortage of Nurses

Mr. J. A. SPARKS asked the Minister the number of nursing staff employed in hospitals at any convenient date in 1938, 1946, and 1948; and to what extent the hospital service was now restricted through shortage of nursing staff.—Mr. BEVAN replied:

September, 1938: 96,800 (including 800 part-time).
September, 1946: 111,600 (2600 part-time).
September, 1948: 132,000 (19,000 part-time).

The number of hospital beds unstaffed in September, 1948, was 57,000 or about a ninth of the total number of beds.

Nurses' Hours

Mr. G. THOMAS asked the Minister of Health whether he would take steps to prevent nurses under 18 years of age being given tours of twelve hours' night duty in public hospitals; and to prevent hospital authorities making compulsory the attendance of nurses at lectures during the nurses' off-duty period.—Mr. BEVAN replied: Guidance on attendance at lectures and off-duty rotas has already been issued to hospital authorities. Guidance on conditions of employment of employees under 18 is in preparation.

National Morbidity Inquiry

Brigadier R. H. RAYNER asked the Minister if he would make a statement on the national morbidity inquiry which he had ordered to be made about all hospital patients.—Mr. BEVAN replied: This inquiry is experimental, is limited to a few hospitals only, and is strictly confidential. Its object is to provide statistical information needed in considering many health problems.

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Obituary

EDMUND IVENS SPRIGGS

K.C.V.O., M.D. LOND., F.R.C.P.

Sir Edmund Spriggs, who died at Ruthin Castle, North Wales, on Feb. 4, was born at Foxton, in Leicestershire, in 1871. He was educated at the grammar school at Market Harborough and when aged 18 was indentured to the late Dr. Lodge, of Rotherham, as a dentist. At the age of 21 he gained a scholarship at Firth College, and from there he went on to Guy's Hospital medical school with an open scholarship. After qualifying with honours in 1896, he was appointed demonstrator in physiology at Guy's, succeeding Gowland Hopkins. Afterwards he went to Heidelberg under Kossel as Gull research scholar and in 1902 published a paper on new methods of estimating pepsin in the gastric juice. After his return to London he was appointed to the Victoria Hospital for Children and the City Road Chest Hospital, and, in 1904, assistant physician to St. George's Hospital, where he soon became dean of the medical school. He settled in London as a consulting physician practising in Bryanston Square. His interest in research continued: in 1906 he delivered the Oliver-Sharpey lectures, before the Royal College of Physicians, on the Bearing of Metabolism Experiments upon the Treatment of Some Diseases, and in 1909 he anticipated the Meulengracht method of giving a relatively liberal diet to patients with peptic ulcer.

Elliott & Fry

Unfortunately Spriggs developed pleurisy in 1910, and though much recuperated after a long holiday he had a severe relapse in 1911 and entered Nordrach-on-Dee Sanatorium for a year. It was there that he came in touch with Dr. David Lawson, who had planned a sanatorium for medical cases other than tuberculosis. Duff House, Banff, was leased and fitted up, and Spriggs became the senior physician. His profound knowledge of clinical medicine, with his background of laboratory research, soon established a reputation for Duff House, which was acknowledged by consultants and medical practitioners throughout Great Britain and Ireland. Spriggs's interests were specially turned to the new advancing knowledge of digestive diseases, and he recruited as co-workers those trained in radiological, laboratory, and dietetic work. He thus laid the foundation for accumulated and accurately observed information on gastric and intestinal diseases, the results of which he published in a series of papers over the next twenty years. Advances in X-ray technique enabled him to give classical descriptions of the diagnosis and treatment of diverticula of the alimentary tract (especially in the colon and duodenum), of gastric and duodenal ulcer, and of cancer of the stomach. Towards the end of the first world war he joined the advisory staff of the Ministry of Food, and besides acting on the central committees he wrote various brochures on dietetics and feeding in war-time for the Government and for the public.

At the end of the war Duff House had become too small to accommodate the patients applying for admission, and the clinic was moved to new and larger quarters in Ruthin Castle, North Wales. During the interruption due to the transfer, Spriggs visited the United States and Canada and studied the advances made in medicine on that side of the Atlantic. He paid a second visit to the States and gave a series of successful lectures there in 1930, when his reputation as an authority on gastro-intestinal disease had been fully established. He made many friends there with whom he continued to correspond.

Besides directing the clinic, Spriggs kept abreast of the progress of medical knowledge. After Banting's discovery of insulin, it was made, tested, and used at the clinic, and Spriggs published an early case of diabetes successfully treated with insulin in 1923. During the daily work of the clinic on cases closely observed and recorded, data were accumulated for the series of papers on gastro-intestinal disorders which have been mentioned. In this he was well served by his colleagues, especially O. A. Marxer whose X-ray work was so accurately done that reproduction of the findings could be introduced into the papers to illustrate the finest detail.

Unfortunately his health broke down again at the end of 1930, but after an illness lasting nearly two years he was able to resume his work with the daily routine of medical cases at the clinic. He published papers on endogenous and exogenous obesity. For his interest was in medicine as a whole. His Croonian lectures to the College of Physicians in 1935 were devoted to a clinical study of headaches based on cases observed at the clinic, and in 1929 he gave a lecture at the opening of the session at his old school, St. George's, on Doctor and Patient, which took a broad and enlightened view of medicine.

The prolonged rest in bed necessitated by his recurring illnesses was used by Spriggs not only to write papers but also to read widely. His tastes were catholic and he had a retentive memory not only for cases he had seen and could relate in detail, but for the famous portions of English and French literature and for the lighter. His Harveian oration, delivered in 1944, was unique in that it was the only one given outside London in man's memory—it was read in Manchester at a special meeting of the Royal College of Physicians on St. Luke's Day in that year—but was also unusual in substance in that he took examples from descriptions of disease in recent fiction written by medical men. Diffident and shy as an undergraduate and young doctor, Spriggs became an excellent raconteur and a pleasing and humorous after-dinner speaker.

Apart from his medical work, he had wide outside interests. In the early days when well he played tennis and golf, and always enjoyed fishing. His favourite sport was shooting, and even when handicapped later by increasing lameness he remained a good shot until the recent war. He took much interest in local good works; he was a justice of the peace in Banff and Ruthin, and recently was chairman of the local juvenile court. He was high sheriff for Denbighshire in 1945. Through his friendship with the first Lord Davies he became much interested in the scheme endowed by Lord Davies and his sisters for the control of tuberculosis in Wales: he was on the council of the Welsh National Memorial Association and house-governor of the sanatorium established at Llangwyfan for North Wales. For these public services and for his medical work Spriggs was made K.C.V.O. in 1935.

Apart from his own ill health, his career was clouded with sorrow. It was a tragedy to himself and his first wife, Miss Alice Watson, of Foxton, whom he married in 1905, when their two adolescent daughters were drowned in a bathing disaster at Banff. Mrs. Spriggs died in 1931, and Sir Edmund later married Miss Janet MacIntosh of Perthshire. After a long illness of nearly two years she died on Feb. 4, a few hours before her husband. In spite of these sorrows Spriggs remained always ready to give his services for others, and he was happy to receive annually at the turn of the year letters and cards from grateful patients scattered far and wide. He retired from active medical work in 1945, but much appreciated being president of the British Society of Gastro-enterologists in 1948, where he was recognised as the doyen of that branch of medicine. He is survived by two sons, both qualified physicians.

GORDON EARLE RICHARDS

M.B. TORONTO, LL.D., F.R.C.P. (C.)

MANY of his colleagues in this country will recall the visit in 1947 to this country of Dr. Gordon E. Richards, director of the Ontario Cancer Foundation, when as Skinner lecturer of the Faculty of Radiologists he discussed at the Royal College of Surgeons the place of surgery and of radiotherapy in the management of mammary cancer.

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Born in Lyn, Ontario, in 1885, the son of Rev. J. J. Richards, he graduated M.B. at the University of Toronto in 1908 with the gold medal. He practised in British Columbia at Prince Rupert and Stewart until 1911 when he moved to New York to study radiology. Later he joined the staff of St. Paul's Hospital, Vancouver, and in 1915 he went overseas to serve with the British forces in the Mediterranean area. In 1917 he settled in Toronto, where he was appointed radiologist to the General Hospital.

This was the beginning of a distinguished career. Dr. Richards applied himself diligently to mastering the physics of radiant energy and its application to the treatment of malignant disease. In this work he ranks among the pioneers. The Ontario Institute of Radiotherapy gave him his opportunity, and over 20 years ago he had the first high-voltage treatment machine and the largest supply of radium in Canada. Tireless in his efforts to perfect methods, his criteria of successful treatment were rigid and high. Over the years he trained many radiologists and they have carried his methods and his zeal for research far and wide. The many honours that came to him included fellowship of the Royal College of Physicians of Canada, honorary membership of the Royal Society of Medicine, and fellowship of the American College of Radiology. In 1946 he was granted the honorary degree of LL.D. by Queen's University, Ontario, and in 1947 he represented Canada in the World Conference on Cancer Research.

"Dr. Richards," writes a colleague, "had an unusual amount of what Crile called 'the kinetic drive.' His hobby was work and his ideal was work carried to perfection. A strong personality, he was esteemed by his staff and his associates. His patients loved him. His lectures and his published papers were lucid and convincing and his teachings will long survive him. He never had time for social relaxation, but he was faithful to his upbringing in his loyalty to his church."

He died on Jan. 13 from leukæmia to which his years of exposure to radium may well have contributed. He is survived by his widow and by two sons, one of whom is also a doctor. A third son was killed while serving in the Canadian Air Force during the war.

H. DAVID HALDIN-DAVIS

B.A., D.M. OXFD, F.R.C.P., F.R.C.S.

Dr. David Haldin-Davis, consulting dermatologist to the Royal Free Hospital, who died at his home at Forest Row on Feb. 2, had a distinguished career in his specialty. His academic distinctions were also of a high order. A scholar of Balliol, he rounded off his life at Oxford with a first-class in the final honours school. He was also president of the Junior Science Club. Continuing his medical studies at St. Bartholomew's Hospital, he qualified in 1905. After holding house-appointments at Barts he became chief assistant in the skin department there, and he was also appointed to the staffs of the City of London Hospital for Diseases of the Chest and Paddington Green Hospital for Children. Meanwhile, in 1908, he had gained the fellowship of the Royal College of Surgeons and the membership of the Royal College of Physicians in the same year. He was elected F.R.C.P. in 1931.

Besides his appointment at the Royal Free Hospital he was also a member of the staff of the Hospital for Diseases of the Skin, Blackfriars, and he served as dermatologist to Willesden district council and the Ministry of Pensions, and as one of the referees of the Ministry of National Insurance.

Dr. Haldin-Davis's wide knowledge helped him to write lucidly and attractively about his specialty for his colleagues. In *Modern Skin Therapy*, in the chapter on the application of X rays in the treatment of tinea tonsurans, of which he had exceptional experience, he gave detailed descriptions of technique which were of great value. In *Skin Diseases in General Practice*, which was first published in 1913 and reached a third edition in 1937, his advice was at once succinct and practical.

His interests extended beyond dermatology and its teaching. His work on hospital planning and building led him to take up enthusiastically the study of housing, recognising the increasing needs of the country for better housing and house-planning. His loyalty to his work at the hospital, his wise counsel at medical committees, and his ready wit endeared him to many who were his colleagues.

In 1924 he married Lily, widow of Frank Samuel, who survives him.

Appointments

COOPER, H. A., M.D. Lond., M.R.C.P., D.P.M.: non-resident psychiatrist, Rainhill Hospital and Whiston County Hospital, Lancs.

GILLIS, LEON, M.B.E., M.B. Witwatersrand, M.CH.ORTH. Lpool, F.R.C.S., F.R.C.S.E., D.L.O.: orthopædic surgeon, St. John's Hospital, London.

HALL, W. F., M.B., B.HY. Durham, D.P.H.: resident surgical officer, Queen Elizabeth Hospital, Gateshead, co. Durham.

HARMER, M. H., M.A., M.B. Camb., F.R.C.S.: asst. surgeon, Royal Cancer Hospital, London.

HOWIE, J. E., M.D. Lpool, D.P.M.: non-resident psychiatrist, Rainhill Hospital and Ormskirk County Hospital, Lancs.

JAMES, G. T., M.B., B.SC. Wales, D.P.M.: non-resident psychiatrist, Upton Hospital and Chester and Birkenhead Hospital.

KAWERAU, EINHART, M.B., M.SC. Dubl.: deputy director and senior lecturer, department of chemical pathology, St. Thomas's Hospital and Medical School, London.

KININMONTH, D. A., M.B. Lpool.: asst. M.O., department of physical medicine, St. Thomas's Hospital, London.

LESTER, G. S., M.B. Birm., F.R.C.S., M.R.C.O.G.: obstetrician in clinical charge, Marston Green Maternity Hospital, Birmingham.

MILLS, W. G., M.B. Birm., F.R.C.S., M.R.C.O.G.: asst. obstetric surgeon to the United Birmingham Hospitals.

MOORE, J. G., B.A., M.B. Dubl., F.R.C.S.E., D.O.M.S.: ophthalmic surgeon, Bolingbroke Hospital, London.

PAGE, W. J. O., F.R.C.S., D.L.O.: asst. E.N.T. surgeon, Cumberland and North Westmorland Special Area Committee and Dumfries and Galloway hospital board.

SANDS, D. E., M.R.C.P.E., D.P.M.: physician-superintendent, St. Ebba's Hospital, Epsom.

SCOTT, O. L. S., M.A., M.B. Camb., M.R.C.P.: part-time dermatologist, Redhill County Hospital, Surrey.

TAYLOR, F. W., M.B. Manc., F.R.C.S.: orthopædic registrar, Hospital of St. Cross, Rugby.

TRAVERS, ELIZABETH, M.B. Manc.: non-resident asst. pathologist, Southport and Ormskirk Hospitals, Lancs.

ZEITLIN, R. A., M.R.C.S.: regional blood-transfusion officer, South London Blood Supply Depot.

Chelsea Hospital for Women, London:

BLAIKLEY, J. B., M.B. Lond., F.R.C.S., F.R.C.O.G.: surgeon.
RICKFORD, R. B. K., M.D. Lond., F.R.C.S., F.R.C.O.G.: surgeon to outpatients.

Manchester Royal Infirmary:

First Assistants to Orthopædic Department:
BOLTON, HAROLD, M.B., B.SC. Manc., F.R.C.S.
CREGAN, J. C. F., M.C., M.B. Lond., F.R.C.S.

Coventry and Warwickshire Hospital:

EVANS, G. R., M.B. Lond., D.L.O.: E.N.T. registrar.
INGHAM, MARGARET, M.B. Birm., D.C.H.: pædiatric registrar.

Births, Marriages, and Deaths

BIRTHS

BAKER.—On Feb. 3, at Hereford, the wife of Dr. W. H. J. Baker—a daughter.

BILLINGTON.—On Jan. 24, at Kampala, Uganda, the wife of Dr. W. R. Billington—a son.

CUTLER.—On Jan. 31, the wife of Dr. Michael Cutler—a son.

HATCHER.—On Jan. 31, in London, the wife of Dr. E. S. J. Hatcher—a daughter.

HUNTER.—On Feb. 3, in Malta, the wife of Surgeon Lieut.-Commander John Hunter, R.N.—a son.

LAURENCE.—On Jan. 29, the wife of Dr. Desmond Laurence—a daughter.

PITT.—On Jan. 12, at Watford, the wife of Dr. N. P. Pitt—a daughter.

SHAW.—On Jan. 26, at Southsea, the wife of Surgeon Lieutenant J. D. F. Shaw, R.N.—a daughter.

SHEPHERD.—On Jan. 31, at Lower Heswall, Cheshire, the wife of Mr. J. A. Shepherd, F.R.C.S.E.—a daughter.

STEWART.—On Jan. 29, at Aldershot, the wife of Major W. M. Stewart, R.A.M.C.—a daughter.

WISE.—On Jan. 29, in London, the wife of Dr. H. T. S. Wise—a son.

MARRIAGES

GIBSON—EVERETT.—On Feb. 4, at Teluk Anson, Malaya, G. A. F. R. Gibson, M.B., to Margaret Ann Everett.

ZEITLYN—MYERS.—On Feb. 3, in London, B. B. Zeitlyn, M.B., to Alice Myers.

DEATHS

BATEMAN.—On Jan. 30, at Chester, Surgeon Commander (D) Albert Brooke Bateman, R.N., V.D., M.B. Lpool, B.D.S. R.C.S.

HALDIN-DAVIS.—On Feb. 2, at Forest Row, Sussex, Haldinstein David Haldin-Davis, M.A., D.M. Oxfd, F.R.C.P., F.R.C.S.

ISARD.—On Feb. 4, Oswald Hanson Isard, M.B. Edin., aged 81.

PARRY.—On Feb. 2, Griffith Wynn Vaughan Parry, M.R.C.S.

SPRIGGS.—On Feb. 4 Sir Edmund Ivens Spriggs, K.C.V.O., M.D. Lond., F.R.C.P.

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Notes and News

OUTPATIENT ARRANGEMENTS

In a circular to hospital authorities the Minister of Health suggests that arrangements for the reception and treatment of outpatients should be overhauled and where necessary reorganised. The main objectives proposed are: (1) the elimination of unnecessary attendances; (2) the reduction of waiting-time to a minimum; and (3) the maximum convenience and comfort of the outpatient. It is pointed out that a patient should not normally be seen without a doctor's letter or a reference from some other responsible quarter; and unnecessary attendances should be eliminated—for example, of patients who before the start of the N.H.S. were permitted to attend because they had no general practitioner. In this way unnecessary pressure on consultative departments can be reduced. Furthermore, all possible steps should be taken "to introduce an efficient appointments system in hospital outpatient departments and clinics as a matter of urgency"; and its operation should be reviewed regularly. The resulting saving of space should make possible the replacement of uncomfortable forms by cheap but comfortable chairs. A canteen should be provided wherever possible; and cleaning and redecoration can do much to improve conditions. The times of clinics should be determined as far as possible by local convenience.

CHANGES IN POISONS LIST AND RULES

In connexion with its earlier announcement of proposed amendment of the Poisons List and Rules (*Lancet*, Jan. 15, p. 129), the Home Office has issued the following observations:

The indication of character which will be prescribed for the labelling of agricultural and horticultural insecticides and fungicides containing dinitrocresols and certain phosphorous compounds is as follows:

"Caution. This substance is poisonous. The inhalation of its vapour, mist, spray or dust may have harmful consequences. It may also be dangerous to let it come into contact with the skin or clothing."

The three paragraphs of the earlier notice referring to rules 18, 30, and 31 of the Poisons Rules, 1935, relate actually to rules 17, 29, and 30.

Rule 30 will not now be amended. Provision will be made in the form of application for its endorsement by the local authority so that the note setting out the law relating to the sale of poisons included in part 2 of the Poisons List (which is part of the form) may be detached and returned to the applicant.

MEDICAL OFFICERS OF SCHOOLS ASSOCIATION

This association's proceedings and report for 1944–47 has now appeared. Besides much useful information it carries 13 addresses given to the association during the years covered. The lecturers include Sir Reginald Watson-Jones on the modern treatment of fractures and injuries, Dr. W. H. Bradley on jaundice, Dr. Wilfrid Sheldon on rheumatism in school-children, Prof. J. A. Ryle on socio-medical surveys, Dr. William Evans on unwarranted cardiac invalidism, Prof. Alan Moncrieff on growth and illness, Sir Adolphe Abrahams on the schoolboy athlete, and Dr. C. H. Andrewes, F.R.S., on influenza in schools. A memorandum on poliomyelitis in boarding-schools is a useful guide to action for headmasters.

A NEW HEARING-AID

The 'Bonochord Duo-Minipak' hearing-aid, manufactured by Messrs. John Bell and Croyden, follows the usual lines of a modern aid. It is made up in a small vestpocket case, and the power is given by a Mallory low-tension battery. In addition, both this and the small high-tension battery can be removed and an adapter fitted in place connected with two larger batteries which must be carried elsewhere. This method of using the instrument prolongs the effective life but does not increase amplification. A crystal insert is supplied. When tested against a 'Medresco' aid it is approximately of the same efficiency—if anything a shade less powerful. Apart from being convertible into the duo-pack type it has no special features.

Association of Army Psychiatrists

The sixth reunion of Army psychiatrists will take place at Slater's restaurant, 18, Kensington High Street, London, W.8, on Saturday, March 19, at 7.30 P.M. Particulars may be had from the hon. secretary, Dr. J. C. Penton, The Old Farm House, 1, Gatehill Road, Northwood, Middlesex.

Royal College of Physicians of London

Prof. H. P. Himsworth will deliver the Oliver-Sharpey lectures on Tuesday and Thursday, March 15 and 17, at 5 P.M., at the college, Pall Mall East, S.W.1. He is to speak on the Syndrome of Diabetes Mellitus.

Royal College of Physicians of Edinburgh

At a meeting of the college held on Feb. 1, with Dr. W. D. D. Small in the chair, the following were elected to the fellowship: R. G. McInnes (Oxford), K. M. Morris (Edinburgh), W. J. Burns (Edinburgh). The diploma of membership was conferred on the following:

W. G. Greene, F. O'D. Finigan, R. Natarajan, Siva R. K. Padmavati, J. M. Barber, F. G. Pattrick, A. M. Merriweather, R. E. Beamish, R. P. Gillespie, S. P. Hall-Smith, J. R. Mackenzie, I. H. Stokoe, R. M. Marquis, D. H. Reilly, J. Williamson, A. W. B. Cunningham, R. G. Mitchell, Alwyce B. Gordon, R. A. Bustamante, G. L. Brinkman.

Hunterian Society

The Hunterian gold medal for 1948 has been won by Dr. Jack Lieber for his essay on the Treatment of Obesity in General Practice. The council have chosen as the subject for the 1949 essay the Treatment of Varicose Veins and their Complications. The competition is open to all general practitioners. Further details may be had from the hon. secretary, Mr. J. C. Ainsworth-Davis, 48, Wimpole Street, London, W.1.

Pharmaceutical Society of Great Britain

On Wednesday, Feb. 16, at 7.30 P.M., at 17, Bloomsbury Square, London, W.C.1, Mr. T. C. Denston, F.R.I.C., editor of the *British Pharmaceutical Codex*, will speak on the National Formulary 1949.

Kent Pædiatric Society

A meeting of this society will be held on Saturday, Feb. 19, at 2.30 P.M. at the Royal Star Hotel, Maidstone, when Dr. Dorothy Makepeace, of the Home Office, and Miss Harvie, children's officer for Kent, will speak on the Children Act. On Saturday, March 5, a meeting for medical members will be held at Farnborough Hospital at 2.30 P.M., when Dr. Charles Baker, of Guy's Hospital, will speak on Congenital Heart Disease.

Manchester Pædiatric Club

This club was inaugurated on March 15 last year with a membership of 25. Dr. Catherine Chisholm was elected president and Prof. Wilfrid Gaisford secretary. At the first meeting on July 7 Prof. Edmond Kerpel-Fronius (Hungary) read a paper on Body Fluids in Dehydration and Malnutrition and Dr. M. L. Thomson followed with Notes on the Use of Arabon in Gastro-enteritis. At the second meeting on Oct. 5 Dr. Dorothy Andersen (New York) spoke on the Treatment of Cœliac Disease. The first annual general meeting was held on Jan. 7 when there was a discussion on Methods of Improving the Child Health Services. At the next meeting on May 9 the lecturer will be Professor Lichtenstein (Stockholm).

Conference on Malignant Disease

A conference on malignant disease of the female pelvic organs will be held in Newcastle-on-Tyne on Friday and Saturday, April 1 and 2, under the auspices of the departments of gynæcology and radiotherapy of the Royal Victoria Infirmary and King's College medical school. The introductory address will be given by Mr. Victor Bonney, and Dr. Malcolm Donaldson, Mr. George Blomfield, and Mr. David Currie will open a discussion on the treatment of carcinoma of the cervix. Other speakers will include Mr. Alan Brews, Dr. A. Glucksmann, Mr. Harvey Evers, and Dr. C. W. Taylor. Further information may be had from Mr. Stanley Way, Royal Victoria Infirmary, Newcastle-on-Tyne.

New Booking-office Window

A new type of booking-office window, designed to prevent the passage of infected breath between passenger and clerk, is being tried at the following railway stations: Bowes Park, Liverpool Street (west office), Marylebone, Grimsby Docks, Watford, Harrogate, Ealing Broadway, Glasgow (Queen Street). The experiment will be watched by medical officers of British Railways in collaboration with the Medical Research Council, and comparative bacteriological tests will be made of the air intake through the present and the new type of window.

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Second Army Medical Services Officers' Reunion

The annual dinner for officers and ex-officers of the R.A.M.C. who served in any formation in Second Army in 1944–45 will be held at Simpson's Restaurant, Strand, London, W.C.2, on March 3 at 7.30 P.M. Brigadier H. L. Glyn Hughes will be in the chair. Applications for tickets should be sent to Dr. R. Gwyn Evans, 33, Sandford Road, Mapperley, Nottingham, or Dr. R. F. G. Ormrod, 4, Aubrey Road, W.8.

Somatotyping

Dr. J. M. Tanner and Dr. Brian Stanford will address the medical group of the Royal Photographic Society, on Thursday, March 3, at 7.30 P.M., on this subject. Somatotyping is a method of studying objectively the physical pattern of the individual, and the lecture will be illustrated by a filmstrip, lantern slides, and a demonstration of photographic technique.

French Information Bureau

The Confederation of the French Medical Syndicates have opened an office at 60, Boulevard de Latour-Maubourg, Paris 7, to supply information to doctors visiting France. The new office, whose French name is Organisation Française d'Accueil du Corps Médical Mondial (O.F.A.M.M.), will help doctors to visit hospitals or attend surgical operations, congresses, and lectures.

Two Scandinavian Films

The Swedish Embassy have lent to the Tavistock Clinic for two months a film called "Morning of Life," dealing with the emerging faculties of the infant. This is a 16 mm. silent film with Swedish subtitles (easily understood) running about 25 minutes. A translation is being prepared. It can be hired, for non-commercial showing only, by educational, medical, and other suitable organisations, on application to the Tavistock Clinic at 2 Beaumont Street, W.1. The Danish Embassy have a 16 mm. copy of Dr. Jarl Wagner Smitt's film, "Determination of Intelligence in Rats by means of the Maze Method," a 17-minute silent film with subtitles in English. Both films were shown at the 1948 International Congress on Mental Health.

Leeds Regional Psychiatric Association

The first meeting of this society was held at the General Infirmary at Leeds on Jan. 29 when 25 psychiatrists from the region attended. Office-bearers were elected, with an executive committee representative of the department of psychiatry of Leeds University, medical superintendents, of mental hospitals and mental institutions, the hospital medical staffs, and psychiatrists in other services or private practice. The objects of the association are to promote and improve the mental health of the individual and the community by the study of clinical, social, educational, and administrative problems of psychiatric practice in the region. Membership is open to specialists in psychiatry and bona-fide trainees who are accepted by the executive committee. Associate membership is open to psychologists, psychiatric social workers, and lay therapists practising in the region. Prof. D. R. MacCalman was elected chairman and Dr. J. W. Affleck hon. secretary.

Congress of Biochemistry

The first International Congress of Biochemistry will be held at Cambridge from Aug. 19 to 25 under the presidency of Prof. A. C. Chibnall, F.R.S. The work of the congress has been divided into the following sections: Animal Nutrition and General Metabolism (chairman, Sir Jack Drummond, F.R.S.); Microbiological Chemistry (Miss M. Stephenson, F.R.S.); Enzymes and Tissue Metabolism (Prof. R. A. Peters, M.D., F.R.S.); Proteins (Mr. K. Bailey, PH.D.); Clinical Biochemistry (Prof. E. J. King, D.SC.); Structure and Synthesis of Biologically Important Substances (Prof. A. R. Todd, F.R.S.); Cytochemistry (Prof. J. N. Davidson, M.D.); Biological Pigments—Oxygen Carriers and Oxidising Catalysts (Prof. D. Keilin, F.R.S.); Hormones and Steroids (Prof. F. G. Young, D.SC.); Chemotherapy and Immunochemistry (Sir Charles Harington, F.R.S.); Plant Biochemistry (Mr. C. S. Hanes, F.R.S.); Industrial Fermentations (Mr. H. J. Bunker). Prof. E. C. Dodds, M.D., F.R.S., is chairman of the executive committee and further information may be had from the honorary organiser of the congress, 56, Victoria Street, London, S.W.1.

Will the Cambridge sender of imperfect pages from last week's LANCET kindly give us his name and address so that his copy can be replaced?

Diary of the Week

FEB. 13 TO 19

Monday, 14th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Mr. H. S. Souttar: John Hunter—the Observer (Hunterian oration.)
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
8.30 P.M. Dr. Trevor Howell, Mr. W. Sampson Handley: Old Age.

Tuesday, 15th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. Marc Daniels: Tuberculosis in Post-war Europe. (First Milroy lecture.)
UNIVERSITY COLLEGE, Gower Street, W.C.1
5.15 P.M. (Physiology theatre.) Dr. A. Schweitzer: Reflexogenic Areas of the Vascular System. (First of five lectures.)
INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5.15 P.M. Dr. I. Muende: Diseases of the Nails.

Wednesday, 16th

INSTITUTE OF DERMATOLOGY
5 P.M. Dr. C. W. McKenny: X-ray Technique.

Thursday, 17th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. Marc Daniels: Tuberculosis in Post-war Europe. (Last Milroy lecture.)
ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. J. G. Bonnin: Diastasis of the Tibio-fibular Syndesmosis. (Hunterian lecture.)
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Dr. A. F. Mahaffy: Epidemiology of Yellow Fever in Central Africa.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, S.W.1
4.30 P.M. Psychiatry lecture-demonstration.
HONYMAN GILLESPIE LECTURE
5 P.M. (Edinburgh Royal Infirmary.) Dr. Clifford Kennedy: Incoördinate Uterine Action.
SOCIETY OF MEDICAL OFFICERS OF HEALTH
5.30 P.M. (B.M.A. House, Tavistock Square, W.C.1.) Dr. C. A. Boucher: Can the M.O.H. Help to Prevent Accidents in the Home?
FACULTY OF RADIOLOGISTS
8.15 P.M. Joint meeting with British Institute of Radiology and R.S.M. section of radiology (32, Welbeck Street, W.1.) Sir Ernest Rock Carling, Dr. Frank Ellis, Prof. W. V. Mayneord, D.SC.: The Physical, Cytological, and Medical Aspects of Protection from Ionising Radiations with special reference to the use of High-voltage X rays and Radio-isotopes. (Meeting will continue on Friday.)

Friday, 18th

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Mr. J. W. S. Lindahl: Place of E.N.T. Surgery in the Treatment of Chest Diseases.
WEST LONDON MEDICO-CHIRURGICAL SOCIETY
7.30 P.M. (South Kensington Hotel, Queen's Gate Terrace, S.W.7.) Lord Horder: ? Guild for Doctors.
BIOCHEMICAL SOCIETY
2 P.M. (St. Thomas's Hospital medical school, S.E.1.) Short papers and demonstration.
MIDDLESEX COUNTY MEDICAL SOCIETY
3 P.M. (Edgware General Hospital.) Demonstration of cases.
ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh
8 P.M. Prof. Robert Walmsley: Anatomical Observations on Congenital Heart Disease.

Lord Webb-Johnson, P.R.C.S., has been made an honorary freeman of the Worshipful Company of Barbers, whose master is Dr. G. G. Macdonald.

Dr. A. D. D. Broughton is standing as Labour candidate in the Batley and Morley by-election.

Dr. Broughton qualified from Cambridge University and the London Hospital in 1929, and took his M.B. Camb. in 1937. He also holds the D.P.M. and the D.P.H. During the war he served with the R.A.F.V.R., afterwards returning to his practice at Batley.

The *Proceedings of the Alumni Association of the King Edward VII College of Medicine, Singapore*, of which the first issue came out last October, will appear from time to time and will include accounts of meetings of the three branches and other news of the association.

CORRIGENDUM: *The Overfed Child.*—In his address to the Devon and Exeter Medico-Chirurgical Society reported in our last issue Dr. John Gibbens did not say that nine-tenths of the diseases of infancy and childhood were due to overfeeding: he said that nine-tenths of the children entering hospital with pneumonia were fat and flabby and that nine-tenths of the babies entering hospital with feeding problems were on full-cream mixtures given in excessive amounts. Nor did he state that more than half of his series of 1500 children had had their tonsils removed: he said that in some years as many as half had undergone tonsillectomy or had notes saying that it was desirable.

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HISTORICAL BUILDING
DES MOINES, IOWA

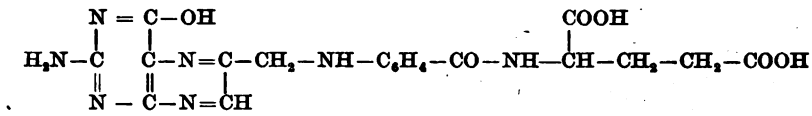
MEGALOCYTIC ANÆMIAS *

JOHN F. WILKINSON
M.D., M.Sc., Ph.D. Manc., F.R.C.P., F.R.I.C.

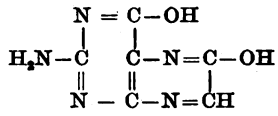
(*Continued from p. 255*)

The Rôle of Folic Acid

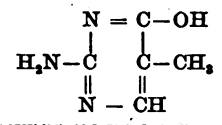
During the last ten years or so, widely varying experiments have indicated that a group of related substances known as "folic acid" and "folic-acid conjugates," vitamins B_c and M, &c., have profound influences on such differing things as the growth of bacteria (*L. casei* and *Strep. fæcalis*), prevention of anæmia in chicks, leucopenia or aplastic anæmia in rats, macrocytic hyperchromic anæmia with leucopenia and granulocytopenia, and sprue-like symptoms in monkeys, &c. (Berry and Spies 1946, Wilkinson 1948). These substances could be isolated from such sources as liver, yeast, kidney, milk, prunes, and green leaves, but Angier et al. (1945) synthesised one "folic acid"—pteroylglutamic acid—which apparently had had profound curative or preventive effects not only in these conditions but also in macrocytic anæmia in man (Spies et al. 1945). This led to enthusiastic anticipation that here at last was the anti-pernicious-anæmia principle or at any rate a very closely related substance. As shown below, it is now clear from clinical observations that pteroylglutamic acid is not (1) the anti-pernicious-anæmia liver factor which is highly potent in very small doses and contains negligible quantities of folic acid; (2) the antineuritic factor (if such exists as a separate entity); (3) the extrinsic factor, since it can be given parenterally without need for hæmopoietin digestion whereas potent sources of extrinsic factor may contain no folic acid; or (4) hæmopoietin, the gastric enzyme.



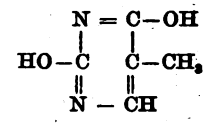
PTEROYLGLUTAMIC ACID ("FOLIC ACID")



XANTHOPTERIN



5-METHYL-ISOCYTOSINE



5-METHYL-URACIL (THYMINE)

Many theories have been put forward in the last two years without much, if any, accurate evidence to support them, and as yet the part played by pteroylglutamic acid is in the realms of pure speculation. Spies et al. (1948) have shown that related or substituted pteroylglutamic acids are either inactive or only slightly active—as with formylpteroylglutamic acid—suggesting a particular specificity of the pteroylglutamic acid molecule as a hæmopoietic agent.

In previous years many other substances, such as constituents of the vitamin-B complex, and various purines and pyrimidines, with and without prior incubation with normal gastric juice or hæmopoietin, have failed in our hands to initiate remissions in test patients with pernicious anæmia.

Following Stokes's (1944) observation that folic acid could be replaced by thymine in the growth experiments using *L. casei*, Spies (1947, Spies et al. 1946) found that 7–15 g. daily was necessary to produce hæmatological and clinical remissions in pernicious anæmia, though its influence on neurological changes, glossitis, and stomatitis was not so good as that of pteroylglutamic acid.

While confirming this, I (Wilkinson 1947) also showed that the related 5-methyl-isocytosine acted similarly in doses of 100–200 mg. daily intravenously or 5 g. by mouth daily, giving slight reticulocytosis and a slight improvement in the red cells and hæmoglobin. Probably larger doses are required for good responses, as in the case of thymine.

It has been shown that xanthopterin, like liver extracts, will cure goat's-milk anæmia in young rats (Tschesche and Wolf 1937) and a form of anæmia produced in salmon and trout by a high-protein diet (Norris and Simmons 1945, Simmons and Norris 1941), though pteroylglutamic acid in this fish anæmia has considerably less activity than has xanthopterin (Mitchell et al. 1944).

On the other hand, xanthopterin would only relieve the hæmatological changes and not the symptoms in monkeys with vitamin-M deficiency; it was thought to produce an increase in the white blood-cells in rats made leucopenic with sulphonamides (Totter and Day 1943, Totter et al. 1944), but these observations have not been confirmed.

Erös and Kúnos (1936) observed that the argentaffine cells were much diminished in number in pernicious anæmia and sprue, and thought they were the source of the anti-pernicious-anæmia factor. Jacobson (1939) suggested that these argentaffine cells in the human intestine probably contained xanthopterin, which might be combined with desoxypentose, and suggested a relationship with hæmopoietin, the anti-pernicious-anæmia stomach enzyme (Wilkinson and Klein 1932).

As already mentioned, I (1940) showed that the villi and crypts of Lieberkühn of the pig's duodenum contained anti-anæmic potency when fed by mouth to patients with pernicious anæmia. The idea of xanthopterin being linked with desoxypentose and the suggestion of Stokes (1944) that folic acid may act in the body to form thymine, which is the essential nucleotide part of the nucleic acid required in cell formation, led me to try the effect of the tetrasodium salt of desoxypentose-nucleic acid on two controlled male patients with pernicious anæmia. The first patient (red cells 1,530,000 per c.mm., Hb 36%) received 20 mg. intravenously daily for ten doses and the second (red cells 1,540,000 per c.mm., Hb 40%) received 50 mg. intravenously daily for ten doses. Neither patient showed any reticulocyte or other hæmatological response after 200 mg. and 500 mg. respectively intravenously.

Now, pteroylglutamic acid occurs abundantly in many foodstuffs but is mainly present in the form of what are termed folic-acid conjugates, which are not universally active until they have been hydrolysed to the parent pteroylglutamic acid by incubation with a suitable enzyme or *Strep. fæcalis*. The two most important conjugates are pteroylheptaglutamic acid (previously known as B_c conjugate or yeast-folic-acid conjugate) which has no effect on the growth of *L. casei* or *Strep. fæcalis*, and pteroyltriglutamic acid (fermentation folic-acid conjugate, fermentation *L. casei* factor), which promotes the growth of *L. casei* but has relatively little effect on *Strep. fæcalis*. Other simpler polyglutamates have been synthesised and utilised. Some of these polyglutamates have profound effects in the treatment of certain deficiency conditions such as can be produced in rats, chicks, monkeys, &c.

On the basis of some as yet inadequate experiments with the natural but not synthetic pteroyl-hepta- or tri-glutamic acids in small doses it has been suggested

* The Oliver-Sharpey lectures delivered at the Royal College of Physicians of London on March 9 and 11, 1948.

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by Bethell et al. (1947) and Heinle and Welch (1947) that pernicious anæmia does not react to these conjugates, owing either to the gastric deficiency of hydrochloric acid and hæmopoietin or to the absence of the anti-pernicious-anæmia liver principle. On the other hand, Spies (1947), Sharp and Vonder Heide (1947), Suarez et al. (1946), and Wilkinson and Israëls (unpublished) have shown that pernicious anæmia responds not only to natural pteroylheptaglutamic acid but also to synthetic pteroyl-di- and tri-glutamic acids. These observations suggest that there are two types of pernicious anæmia, but there is certainly no clinical or other experimental evidence to support this idea.

Again, it was shown by Sharp et al. (1944) and Sharp and Vonder Heide (1947) that a big increase in urinary pteroylglutamic acid took place in pernicious anæmia after treatment with natural pteroylheptaglutamic acid, at the same time demonstrating the unreliability of the excretion values. On the other hand, Bethell et al. (1946) and Welch et al. (1946) did not observe such increase in the urine after administration of folic-acid conjugate.

It must not be overlooked that, according to Denko et al. (1946), large amounts of pteroylglutamic acid can be synthesised in the gut of man as well as of other animals. Further and more definite evidence will no doubt be forthcoming when supplies of synthetic pteroylheptaglutamic acid are obtainable.

In the meantime, therefore, any theories depending on the assumption that pernicious anæmia is due to an inability to convert pteroylpolyglutamic acids to the free pteroylglutamic acid must be suspect. Nor is there any unequivocal evidence to support the idea that liver extracts contain a "liberating factor" which enables the polyglutamates to be reduced to the free pteroylglutamic acid as an important step in hæmopoiesis—in fact the evidence is against this idea—otherwise, why the hæmatological and neurological relapses and failure to regain normal blood-counts when synthetic folic acid is given?

Again, pteroylglutamic acid can be liberated from its conjugates (the pteroylpolyglutamic acids) by the action of certain specific enzymes—the conjugases—and it has been shown experimentally that liver, kidney, yeast, and bone-marrow contain substances capable of inhibiting this enzyme reaction because their affinities for the conjugases are greater than those of the pteroylpolyglutamic acids. Thus, the glutamic-acid polypeptide of *p*-aminobenzoic acid has an affinity ten times greater than that of the pteroylheptaglutamic acid for the conjugase present in rat liver (Ratner et al. 1946). It has therefore been suggested that in pernicious anæmia the fault may be a partial or complete inability to inactivate such inhibitors of conjugases.

Now, certain obvious facts cannot be ignored: pteroylglutamic acid does not maintain the majority of patients with pernicious anæmia in normal health; it does not eliminate macrocytosis or prevent a gradual fall in the blood-count, even with increasing doses; its effective dose is 5000–20,000 times greater than that of liver principle; and, most important of all, it does not prevent or relieve neurological changes—rather does it appear to precipitate their onset (Wilkinson 1948). For these reasons we are forced to conclude that pteroylglutamic acid probably does not play a major or essential part in the normal hæmopoietic mechanism. It may have some subsidiary or independent rôle, or it may just be a more powerful type of hæmopoietic stimulant and nothing more.

Classification of Megalocytic Anæmias

In pernicious anæmia there is a permanent irreversible achylia gastrica with a failure of the stomach to secrete hæmopoietin, whereas in achrestic and other megalocytic anæmias gastric secretion may be normal.

The liver in relapsed pernicious anæmia does not contain the so-called anti-pernicious-anæmia liver principle, but this is remedied after adequate treatment. The same or similar anti-pernicious-anæmia liver principle is present in the livers of normal people and in patients with achrestic, aplastic, and other anæmias as well as in livers of very many mammals, fish, &c. The bone-marrow in megalocytic anæmias like pernicious anæmia and achrestic anæmia shows an active megaloblastic hyperplasia which can be readily identified by sternal-marrow biopsy. In pernicious anæmia it returns rapidly to normoblastic hyperplasia after correct treatment.

It is clear that the anti-pernicious-anæmia liver principle is essential for the proper maturation of the pro-erythroblasts in the marrow via normoblasts to normal erythrocytes (Israëls 1939). Thus, for the production and maintenance of normal red cells in the circulation and for the prevention of megalocytic anæmias such as pernicious anæmia, at least one essential factor is the presence of the liver anti-pernicious-anæmia principle in the body, and its availability for use as required by the hæmopoietic tissues. The supply of this factor depends on its normal production by the interaction of hæmopoietin and extrinsic factor in the stomach, followed by absorption of the formed liver principle into the blood-stream—i.e., the mechanism is not one solely affecting the hæmopoietic system but also involving the gastro-intestinal system, and I look on it as a gastro-hæmopoietic mechanism. It was on this basis that I classified megalocytic anæmias as follows (Wilkinson 1936a):

Megalocytic (Megaloblastic) Anæmias

(1) *Achylic Megalocytic Anæmias:*
Extrinsic factor not deficient; pepsin, hydrochloric acid, and hæmopoietin absent; anti-anæmic liver principle deficient; permanent treatment necessary:
- (A) *Atrophy of mucosa* (hæmopoietin, &c., not secreted): Pernicious anæmia
- (B) *Artificial, acquired deficiency:*
  - (*a*) *Destruction of hæmopoietin:* Gastro-enterostomy anæmia
  - (*b*) *Destruction or removal of hæmopoietin-secreting glands:* Gastrectomy anæmia; Gastric mucosal destruction (fundus and cardia) by corrosive poisons, gastritis (toxic, alcohol, syphilis, tuberculosis).

(2) *Hepatic Megalocytic Anæmias:*
Extrinsic factor, hydrochloric acid, pepsin, hæmopoietin, and anti-anæmic liver principle present; cause unknown; treatment unsatisfactory:
Achrestic anæmia
Liver-cirrhosis anæmia

(3) *Secondary Megalocytic Anæmias:*
- (A) Hydrochloric acid, pepsin, hæmopoietin usually present; cause identified; usually cured by treatment:
  - (*a*) *Dietetic:* Starvation; Tropical anæmia; Ulcer dietary
  - Gastro-enterostomy
  - Intestinal parasites
  - (*b*) Sprue; Cœliac disease; Idiopathic steatorrhœa; Multiple intestinal stenoses; Gastro-intestinal fistulæ
  - (*c*) Megalocytic anæmia of pregnancy
- (B) Hydrochloric acid, pepsin, hæmopoietin, extrinsic factor present; treatment unsatisfactory:
  Hepatitis; Pancreatitis; Nephritis; Syphilis; Tuberculosis; Radiation anæmias

Gastro-hæmopoiesis

In the mechanism of gastro-hæmopoiesis there are two main phases for normal red blood-cell production, extramedullary and intramedullary.

Extramedullary Phase.—This is concerned with the normal formation in the alimentary tract of the anti-anæmic liver principle from the extrinsic factor in the food and hæmopoietin in the stomach, its absorption from the gut, transport, and delivery to the bone-marrow as follows (see also table I):

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TABLE I—MEGALOCYTIC ANÆMIAS

Deficiency	Extrinsic factor	Hæmopoietin	Hæmopoietic activity of liver		Bone-marrow	Disease
			Before treatment	After treatment		
Extrinsic factor	0	+	0	+	Megal. hyperpl.	Dietetic deficiency
Hæmopoietin	+	0	0	+	,,	Pernicious anæmia
Incubation reaction ..	+	+	0	+	,,	..
Absorption ..	+	+	0	+	,,	Intestinal disease
Storage ..	+	+	0	0	,,	Liver disease
Utilisation ..	+	+	+	+	,,	Achrestic anæmia
Destruction ..	+	+	+	+	Normobl. hyperpl.	Hæmolytic anæmia

Failure of Extramedullary Gastro-hæmopoiesis

(1) *Deficiency of Extrinsic Factor:*
Starvation, or incorrect diet
Ulcer dietary
"Tropical" anæmia

(2) *Deficiency of Hæmopoietin:*
Pernicious anæmia,
Achylic megalocytic anæmias: Destruction of mucosa
Removal of mucosa
Destruction of hæmopoietin

(3) *Failure of Reaction:*
Gastro-enterostomy
Parasites (?)

(4) *Lack of Absorption of Anti-anæmic Principle:*
Sprue
Steatorrhœa
Parasites (?)
Intestinal obstruction or stenosis

(5) *Complete or Partial Lack of Storage of Anti-anæmic Principle:*
Megalocytic anæmia of pregnancy
Cirrhosis

(6) *Lack of Utilisation of Anti-anæmic Principle:*
Achrestic anæmia

Consequently, there are the following stages:

(1) *Dietetic*, in which the extrinsic factor is supplied in the food to the stomach.

(2) *Gastro-intestinal*, where the extrinsic factor is mixed and digested with the hæmopoietin in the stomach (secreted mainly by the human fundus), leading to the enzyme reaction which forms the anti-pernicious-anæmia liver principle or its precursor, which is finally absorbed from the intestinal tract through the intestinal mucosa into the blood-stream.

(3) *Intravascular*, in which short stage the absorbed anti-pernicious-anæmia principle is transported in the portal blood-stream to the

(4) *Visceral depots*, where the anti-pernicious-anæmia liver principle is stored mainly in the liver until it is required for red-cell formation. Then it is mobilised from these stores and carried by the systemic blood-stream to the bone-marrow.

Probably the incubation product produced in the stomach is the fully formed anti-pernicious-anæmia liver principle, but the possibility cannot be ruled out that a precursor may be the first product, which either in course of its passage through the alimentary tract or intestinal mucosa or during storage in the liver is ultimately elaborated into the final substance now extracted from the liver as the so-called anti-pernicious-anæmia principle.

Intramedullary Phase.—This phase represents the intramedullary mechanism whereby the hæmopoietic tissues elaborate the normal red cells from the pro-erythroblasts, via the early intermediate, and late normoblasts, as suggested by Israëls (1941) working in my department.

Achrestic Anæmia

The question of achrestic anæmia (Israëls and Wilkinson 1936, 1940) requires special consideration, since a few criticisms in the past indicate a misunderstanding of the condition and an incorrect reading of our description and its differential diagnosis, and there seems to be some confusion in terminology.

It is well known that other blood dyscrasias may simulate pernicious anæmia very closely—e.g., leukæmia, hæmolytic anæmia of pregnancy, "pseudo-aplastic" anæmia, chronic hæmolytic anæmias, achrestic anæmia, sprue, idiopathic steatorrhœa, &c. As a rule a careful examination of the blood, gastric juice, and bone-marrow will differentiate these. When a patient with a severe hyperchromic anæmia does not respond to adequate hæmopoietically active treatment for pernicious anæmia he has usually one of the following conditions: true aplastic anæmia, "pseudo-aplastic" anæmia, acute or "aleukæmic" leukæmia, or achrestic anæmia. Sternal biopsy distinguishes between these, for in true aplastic anæmia the marrow is fatty and the cells are relatively few; in "pseudo-aplastic" anæmia cells are numerous, the red-cell types being mostly normoblasts of various types with perhaps a very few pro-erythroblasts; in acute or "aleukæmic" leukæmia the marrow may be packed with immature leucocytes; and in achrestic anæmia there is a typical megaloblastic hyperplasia like that seen in pernicious anæmia (table II). Pseudo-aplastic anæmia, though still rare, is probably the commonest of these conditions, and achrestic anæmia the one least often seen.

Israëls and I have seen 14 cases of achrestic anæmia, during which time I have seen 1600 cases of pernicious anæmia—a very low frequency of 1 case of achrestic anæmia to every 114 cases of pernicious anæmia. Hence we cannot expect to see many cases of achrestic anæmia except in large groups of cases of megaloblastic anæmia.

The features of achrestic anæmia are as follows: a blood picture exactly resembling that of pernicious anæmia, with a typical addisonian megaloblastic marrow either at biopsy or at necropsy; no involvement of the neurological system; no gastro-intestinal symptoms; and no evidence of hæmorrhages, toxic factors, or liver disease. The gastric juice usually contains free hydrochloric acid, pepsin, and hæmopoietin; and, though the livers at necropsy contain large amounts of the anti-pernicious-anæmia liver principle, the patients show progressive, finally total, failure to respond to anti-pernicious-anæmia treatment. We consider that the ætiological factor is a failure or inability to utilise the anti-pernicious-anæmia principle or to mobilise it from the depots in the liver (Wilkinson and Israëls 1935).

Other examples of this anæmia have been described by Abrahamson and Thompson (1937), Dameshek and Valentine (1937), Davidson (1948), Davidson and Fullerton (1938), Falger (1946, 1947), Huse (1944), Hynes (1939), and Wauchope and Leslie-Smith (1938). An attempt was made (Vaughan 1936, Mogenson 1938) to class achrestic anæmia as a megalocytic anæmia due to liver disease, but at necropsies we have not detected any lesion in the liver to support this, and we have grave doubts whether megalocytic anæmia in liver disease is associated with megaloblastic changes in the marrow. The condition is not related to the hæmolytic anæmias, which show normoblastic hyperplasia of the marrow (table II) (Israëls 1939, Scott 1939).

The main difficulty appears to be the unnecessary confusion between achrestic anæmia and aplastic or "pseudo-aplastic" anæmia (Castle and Minot 1936, Zanaty 1937, Wilkinson and Israëls 1937, 1938, Israëls and Wilkinson 1938, Davidson and Fullerton 1938, Schulten 1939, Heilmeyer 1942). Aplastic anæmias may occasionally show a hyperplastic marrow, which may be patchy or widespread, but in progressing cases diminution of erythropoiesis is seen later; megaloblasts are not seen in the marrows of these cases. Pro-erythroblasts or early normoblasts ("macroblasts" of Naegeli) may be seen in small bunches, but the whole marrow

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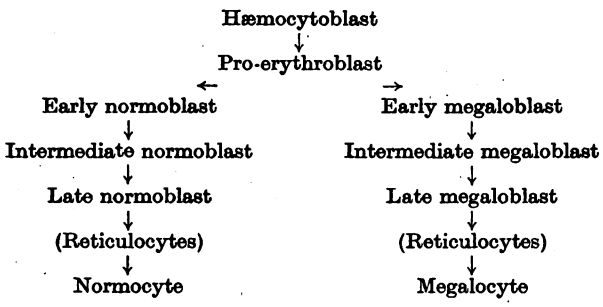
picture differs entirely from that of achrestic anæmia, in which it is almost identical with that of pernicious anæmia—a typical megaloblastic hyperplasia. Further, the term "megaloblast" is confined to a series of cells with distinctive nuclear structure seen in pernicious anæmia in relapse. They do not take part apparently in normal red-cell formation in extra-uterine life, for this takes place solely by maturation of the normoblasts.

Israëls (1939, 1941) has suggested that the two have a common ancestor, the red blood-cell development being according to the following scheme:



Israëls divides morbid erythropoiesis into four types with different bone-marrow pictures, and these four types correspond to different clinical and ætiological groups. The type in which there is a megaloblastic erythropoiesis can be sharply distinguished from others, since the megaloblasts are easily recognised in sternal-puncture material. The corresponding clinical types are true pernicious anæmia, achrestic anæmia, and some cases, but not all, of sprue and nutritional macrocytic anæmia.

Experiments have made it clear that it is only in this group that the anæmia will respond to the anti-anæmic liver principle, desiccated stomach preparations, or folic acid; achrestic anæmia sometimes gives a partial response, sometimes it is completely refractory.

Minimal doses of hæmopoietically active material can bring about a change from a megaloblastic to a normoblastic marrow picture within 48 hours, and this may happen, especially in the nutritional types, even when the succeeding rise in the number of red cells and in the percentage of hæmoglobin is relatively small. Hence the vital importance of sternal-marrow biopsy before any treatment is given, to avoid the difficulty of assessing the value of liver, stomach, or folic-acid treatment if this is not done.

The adoption of these ideas is reflected in the present nomenclature: we tend now to speak of megaloblastic anæmia and not merely macrocytic or megalocytic anæmia. It has also been shown that large red cells can be found in some anæmias with purely normoblastic marrow, not related at all to the megaloblastic group; such cases do not respond to liver and stomach, and there is little doubt that they formed many of the so-called refractory cases in the earlier reports. In table II I have summarised the main features of these anæmias and compared them with those found in aplastic and hæmolytic anæmias.

TABLE II—COMPARISON OF ANÆMIAS

Character	Pernicious anæmia	Achrestic anæmia	Nutritional megalocytic anæmia	Megalocytic anæmia of pregnancy	Aplastic anæmia	Hæmolytic anæmia
Age (years)	40–70 (87%)	20–70	Any	20–45	Any	Any
Onset	Insidious	Insidious	Insidious	Rapid	Rapid	Rapid
Colour	Lemon yellow	Slightly yellow	Pale	Slightly yellow	White	Very yellow
Glossitis	50%	Nil	+	Nil	Nil	Nil
Flatulence and dyspepsia	59%	Nil	+	Occasional	Nil	Nil
Diarrhœa	21%	Nil	+	Occasional	Nil	Nil
Constipation	42%	Nil	Nil	Occasional	Nil	Nil
Neurological symptoms	Common	Nil	Nil	Nil	Nil	Nil
Hæmorrhages	Occasional	Nil	Occasional	Nil	Common	Occasional
Hepatomegaly	16%	Nil	Nil	Nil	Nil	Occasional
Splenomegaly	33%	Occasional	Nil	Nil	Rare	Common
Red blood-cells	Megalocytic hyperchromic	Megalocytic hyperchromic	Megalocytic hyperchromic	Megalocytic hyperchromic	Normocytic normochromic	Megalocytic or normocytic hyperchromic
Reticulocytes	Few (increased in remission)	Few (increased in remission)	Few	Few	Few or nil	Numerous
Red-cell fragility	Normal	Normal	Normal	Normal	Normal	Often increased
Gastric secretion (HCl)	Nil	Normal	Normal	Normal or diminished	Normal	Normal
Hæmopoietin	Nil	Normal	Normal	Normal or diminished	Normal	Normal
Diet deficiency	Nil	Nil	Present	Present	Nil	Nil
Marrow	Megaloblastic hyperplasia	Megaloblastic hyperplasia	Megaloblastic hyperplasia	Megaloblastic hyperplasia	Normoblastic aplasia or hypoplasia	Normoblastic hyperplasia
Anti-P.A.-factor in liver	Nil	Present	?	Nil or diminished	Present	Present
Response to treatment:						
Liver	Very good	Poor	Very good	Very good	None	None
Stomach	"	"	"	"	"	"
Folic acid	Good (?)	? (+)	"	"	"	"
Prognosis	Very good	Poor	"	"	Very poor	Very good (splenectomy)

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Results of Treatment and Prognosis

Since the introduction of the liver-diet treatment (Minot and Murphy 1926) and of hog's-stomach therapy (Wilkinson 1929), treatment of pernicious anæmia has been well standardised; good results with adequate treatment have often been reported from other large clinics besides my own in Manchester. Properly administered, both hog's stomach and liver extracts are highly effective, the former as a desiccated powder given by mouth, and the latter as extracts for use by mouth or by parenteral administration.

In my series 441 patients were treated with only stomach preparations and 513 with only liver extracts of different types, the remainder having received mixed treatments. Out of 1480 patients so treated only 301 have died in the last nineteen years, the remaining 1179 being alive and well now. Relapses were few, if the patients were rigidly controlled in clinics specially run for this purpose, but from our experience a few essential points must be emphasised. It is essential to make a correct diagnosis before starting treatment, which may obscure the blood picture. Both patient and doctor must be impressed that the disease requires permanent and regular treatment if the patient is to remain well, but it is not cured. I have seen too many patients who have had their treatments stopped because a normal blood-count had been attained. Blood-counts should be done at least every 3–6 months. Longer intervals often mean that the patient relaxes treatment and relapses, or, omitting to attend, dies in the interval from relapse, subacute combined degeneration of the cord, or intercurrent disease. Regular observation of these patients should reveal when any slight changes in symptoms indicate the early stages of a complicating disease such as neoplasm, diabetes, hyperpiesis, &c. Many of my patients developing, for example, cancer of the stomach have complained of unusual recurrences of indigestion and anorexia or loss of weight, indicating the need for further investigation; and an unusual polyuria and loss of weight have suggested diabetes; and so on.

Excluding the complications, my patients have done extremely well, and with proper and adequate treatment none has failed to respond to treatment; nevertheless, I noted a tendency during the latter half of the war for patients on liver extracts alone to lose some weight and to require greater quantities of liver extracts to maintain their blood-counts. The addition of hog's stomach (14–28 g. daily) solved this problem, which was apparently due to inadequate protein in the diet. Liver extracts are often given in too small a dosage for proper maintenance—perhaps a consequence of the claims for the efficacy of minimal amounts of particular commercial liver extracts. No patient should go for more than two or three weeks without an injection of liver extract of any type, but often it may be needed more frequently. Where cord changes are present, full doses of liver extract should be given weekly or twice weekly, but stomach preparations are undoubtedly the treatment of choice. The administration of liver extracts by mouth is expensive, wasteful, and usually not indicated except in liver-sensitive patients. In considering dosage of liver extracts one must remember the lower post-war potency of these, due partly to the use of "pharmaceutical" livers (see above). Hog's stomach, pyloric, or duodenal preparations, in my experience, give better and more reliable results and are certainly the best of all forms of treatment for patients with subacute combined degeneration of the cord. These preparations supply not only 28 g. of protein additional to the ordinary meat ration but also the anti-pernicious-anæmia stomach principle hæmopoietin in good quantity, the extrinsic factor in the muscle myoglobulin, and some anti-pernicious-anæmia liver principle preformed by the interaction of the first two during the preliminary stages of desiccation. Good preparations also contain pepsin and some combined hydrochloric acid, thus dispensing with the need for the hydrochloric-acid and pepsin mixture usually prescribed for these patients. Desiccated hog's stomach is best given initially in doses of 10 g. three times daily with meals; it must not be heated at any time, since this inactivates the hæmopoietin.

No case treated adequately in my clinics with active hog's stomach or parenteral liver preparations has developed subacute combined degeneration or shown any worsening if it was originally present, but in most the neurological changes have shown much improvement. Only those older patients with severe subacute combined degeneration of the cord have shown less marked improvement in the neurological aspects. Thus, in a group of 441 consecutive patients treated for 6 years with hog's stomach only 14 died (4 of bronchopneumonia, 3 of cardiovascular disease, 2 of subacute combined degeneration of the cord, and 1 each of other diseases), and 15 who had relapsed owing to laxity in treatment recovered when again put on full doses of desiccated stomach. No case initially free developed cord changes. This has been my experience throughout the last nineteen years.

The greatest difficulty I find is to get adequate supplies of pig's stomach, which apparently are now being diverted to the manufacture of meat pies and sausages rather than to the relief of a fatal disease.

LIVER-REFRACTORY MEGALOBLASTIC ANÆMIAS

In the last twenty-two years many thousands of cases of pernicious anæmia have been treated with liver and stomach preparations, and very rarely have cases been reported as not responding to treatment. Recently, however, a few reports have appeared, almost all in Britain, describing what are termed liver-refractory megaloblastic anæmias and liver-refractory pernicious anæmia in surprisingly high numbers for the sizes of the clinics and certainly in striking contrast to the experiences of ourselves and others.

In my own clinic I personally have seen over 1600 cases of pernicious anæmia, and I can say that in none of the uncomplicated cases have I seen a liver-refractory (megaloblastic) pernicious anæmia develop. Relapses occur only through discontinuance of, or inadequate, treatment, treatment with inactive liver preparations, or the onset of severe complications (see below). On the other hand, I have often had referred to me as liver-refractory cases patients who have been treated sometimes with very large doses of highly purified liver extracts without response. In practically all these cases the liver extract concerned has been prepared by the Dakin and West or a similar method, which, as I have already indicated, often gives batches of reduced or negligible potency. These patients have always responded to ordinary standard liver extracts in normal dosage (fig. 3; Wilkinson and Israëls 1947), a fact which confirms my view that most of these cases of refractory pernicious anæmia are really only refractory to inactive highly purified liver preparations. The solution is obvious. This is not only my own experience—many others have made and are making similar observations. It is clear that either such preparations are not being tested adequately before issue (the clinical test is the only reliable one at the present time), or only some batches are being tested, or some accessory factor has been removed, or the preparation does not remain active after issue. The last is unlikely, since I have found that liver extracts will maintain potency for many years when stored in sealed ampoules. The testing of liver extracts must be done under rigidly controlled conditions, and at least two or three patients must be used to test each batch of extract to eliminate errors, spontaneous remis-

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sions, and differences in sensitivity in test patients (see above). In practice, therefore, one must be on guard against these causes of failure with liver extracts. If one preparation does not produce the expected responses within two weeks it should be changed and another preparation tried before the case is labelled as refractory.

The efficacy of good and adequate treatment of pernicious anæmia has been reported repeatedly by many observers. In addition to my own extensive series, I draw attention to the views of Bohn, Decastello, Denecke, Francke, Heilmeyer, Hoff, Nonnenbruch, Rohr, Schilling, Schulten, Seggel, and Voit who stated in 1942 that they had never seen patients with liver-refractory pernicious anæmia in their clinics. Klima (1942) saw one case of pernicious anæmia which did not respond, and Bohn (1942) saw such cases only in complications such as gastric cancer and coli bacilluria.

There is far too great a tendency these days for a patient who does not respond to treatment with an intramuscular liver extract to be labelled "refractory" and then treated with some oral preparation such as proteolysed liver, remarkable therapeutic claims afterwards being made for the latter. If the patient shows all the typical features of pernicious anæmia—megalocytic anæmia, megaloblastic marrow, and achlorhydria—the term "refractory" is unjustified from the point of view of classification and prognosis, unless the anæmia has not responded to another liver preparation of which the actual batch used is known to be active by previous test. The fact that a particular batch of liver has been found to be active on one occasion does not imply that subsequent batches will be active; as I have repeatedly stated, every batch of liver extract issued for general use must be clinically tested before issue, and in all investigational work, as is our practice, known active liver batches should be kept on hand specially for checking the responses of these so-called refractory cases of pernicious anæmia. If this were done, I am convinced, as are many others, that refractory pernicious anæmia would disappear, and the unfortunate results experienced by very many general practitioners with these highly purified Dakin and West types of liver extracts of variable potency would not arise.

(To be concluded)

THE TREATMENT OF TYPHOID CARRIERS WITH PENICILLIN AND SULPHATHIAZOLE *

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Bigger (1946) demonstrated the synergic action in vitro of penicillin and sulphathiazole on *Salmonella typhi* and recommended their use in typhoid fever. Thomas and Hayes (1947) confirmed Bigger's findings, and McSweeney (1946) reported favourable results with this method of treatment.

Many workers have recorded the high concentration of penicillin in the urine of patients undergoing treatment. The sulphonamides are also excreted in the urine. Rammelkamp and Helm (1943) showed that penicillin was concentrated in the liver and excreted in the bile. Zaslow et al. (1947) showed that, in general, the penicillin level in the gall-bladder bile soon after parenteral injection was equal to, or slightly greater than, that in the blood, and that penicillin entered the gall-bladder via the cystic duct.

Since typhoid carriers harbour the organisms in either the biliary or the urinary tracts, or in both, it seemed worth investigating the possibility of curing the carrier condition with penicillin and sulphathiazole. Accordingly fifteen male typhoid carriers, inmates of Irish mental hospitals, were transferred to Grangegorman Mental Hospital, Dublin, where treatment was given.

PRELIMINARY INVESTIGATION

Cultures of fæces and urine were made on Wilson and Blair's medium (Difco 'Bacto' bismuth sulphite agar), on Hynes's modification of Leifson's medium, and in tetrathionate broth followed by Wilson and Blair's medium. Pure cultures were obtained from subcultures made from each medium on MacConkey's medium, and the identity of the strains of *S. typhi* isolated was established in the usual way.

The superiority of the Wilson and Blair-MacConkey and the tetrathionate broth-Wilson and Blair-MacConkey combinations over Leifson-MacConkey was so evident that all further investigations were carried out with these two combinations.

Ten of the fifteen carriers were selected for the trial, mainly on the basis of the constancy with which they excreted *S. typhi*. Of the ten, whose average age was fifty-seven, none had been a carrier for less than one year: the average duration of the carrier state was four years. *S. typhi* was isolated on 5, 6, or 7 occasions from 8 consecutive daily specimens of fæces of each patient. Six were also urinary carriers, *S. typhi* being isolated on 1, 2, or 4 occasions from 8 consecutive daily specimens of urine. The organism was not isolated from any of the 8 specimens of urine obtained from the remaining four patients, who were therefore not regarded as urinary carriers.

Three of the strains of *S. typhi* isolated were of phage type E; the remaining seven were untypable. The ten strains of *S. typhi* showed minor differences in their sensitivity to the combination of penicillin and sulphathiazole, but all were killed by concentrations which, it was believed, were attainable in the blood of patients undergoing intensive treatment. The agglutinin titres of the serum of each patient for H, O, and Vi suspensions were determined. H titres (Dreyer method) varied from 1 : 25 to 1 : 2500; O titres from 1 : 80 to 1 : 640; and Vi titres (Felix method) from 1 : 5 to 1 : 80. Wide variations in the three titres of an individual serum were observed—e.g., H 1 : 250, O 1 : 160, Vi 1 : 5; H 1 : 25, O 1 : 640, Vi 1 : 80; and H 1 : 25, O 1 : 160, Vi 1 : 20.

TREATMENT

The ten patients were treated as follows:

An initial dose of sulphathiazole 2 g. was given by mouth, followed by 1 g. three-hourly until 52 g. had been given. Six hours after the first dose of sulphathiazole, penicillin 600,000 units was injected intramuscularly, followed by 600,000 units three-hourly until 30,000,000 units had been given. Treatment lasted $6^1/_2$ days. The penicillin used was Glaxo sodium penicillin, the labelled potency of which was 1350 units per mg. Each dose was dissolved in 2·5 ml. of sterile glass-distilled water. The patients did not complain of pain after the injections.

The concentration of penicillin in the sera of the treated patients (with one exception) was 8–14 units per ml. 5 min. after an injection, and 1·1–5·2 units per ml. 2 hours and 55 min. after an injection. In no case did a specimen of urine examined during treatment contain less than 1000 units of penicillin per ml. In the exceptional case referred to above the serum contained 80 units of penicillin per ml. 2 hours and 55 min. after an injection, and 3·8 units per ml. 2 days after the last injection. This patient had advanced kidney disease,

* An investigation carried out in the department of bacteriology, Trinity College, Dublin, and in Grangegorman Mental Hospital, Dublin, under a grant made from the Guinness Fund of the Medical Research Council of Ireland.

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which caused her death 40 days after the end of treatment.

The sera of three patients under treatment were tested for their power of inhibiting the growth of the strains of *S. typhi* isolated from the same patients. In two cases a 1 : 8 dilution, and in the third a 1 : 32 dilution, of the serum in broth completely inhibited the growth of the homologous strain of *S. typhi*.

Details of the results obtained with these ten patients are given below. For the moment it suffices to say that what is believed to be a cure resulted in only one case. One patient died after treatment, before it could be asserted with certainty that she had been cured of the carrier condition.

The relative failure of the treatment might have been due to insufficient dosage of penicillin, inaccessibility of the organisms to the drugs, the development of penicillin-resistant strains, or the presence of persisters (Bigger 1944). Radiographic investigation of four patients suggested the presence of a calculus in the biliary tract of one, and a very poor concentration of dye in the bile in the Graham Cole tests of two; but, owing to the uncoöperative attitude of the patients, this type of investigation was not entirely satisfactory. Investigation of the sensitivity to penicillin and sulphathiazole of strains isolated before and after treatment showed that in only one case had there been any significant increase in their resistance, and that, even in this case, resistance was not sufficiently high to rule out the possibility of successful treatment.

It was decided to re-treat four of the patients in whom the first treatment had failed, and in their case to increase the duration of treatment, so that the total dose of penicillin would be much higher, and to give it intermittently to deal with persisters. The following scheme was adopted:

Treatment was carried out with the same dosage and timing of sulphathiazole and penicillin as in the first trial but was continued for only 3 days. Four such treatments, each of 3 days' duration, were given with intermissions of 2, 3, and 4 days between each. The total period of treatment covered 21 days, during which each patient received sulphathiazole 100 g. and penicillin 57,600,000 units.

During treatment, one of the patients became ill and, since it was believed that the treatment was adversely affecting her, it was stopped. Only three patients remain, therefore, for consideration.

The criterion of cure decided on before the trials began was strict. It was believed that the carrier condition might, with a high degree of probability, be regarded as cured if, over a period of a year after the end of treatment, 35 specimens of fæces and of urine, on culture on Wilson and Blair's medium and in tetrathionate broth, did not give any growth of *S. typhi*. It was decided that specimens should be examined, beginning on the 3rd day after the end of treatment, daily for 10 days, on alternate days for 10 days, once a week for 6 weeks, once a month for 9 months, and, about 12 months after the termination of treatment, daily for 5 days.

This scheme was carried out with, during the later stages, only such minor departures from the time-table as were occasioned by the necessity of avoiding weekends and holidays. Examinations were made according to the scheme in the case of all patients who completed treatment (except the one who died) until either a positive result had been obtained or about 12 months had elapsed.

TABLE I—RESULTS OBTAINED WITH CONTINUOUS TREATMENT

(Sulphathiazole 52 g. and penicillin 30,000,000 units in 6½ days)

Case no.	Isolation of *S. typhi*					
	Fæces			Urine		
	No. of specimens negative	Last day after end of treatment on which a negative result was obtained	First day after end of treatment on which a positive result was obtained	No. of specimens negative	Last day after end of treatment on which a negative result was obtained	First day after end of treatment on which a positive result was obtained
3	17	35	—	17	35	—
	(Patient died 5 days after last examination)					
4	3	5	6	4	6	7
5	8	10	11	22	95	—
7	7	9	10	12	16	18
8	9	11	12	14	20	22
9	35	384	—	12	384	—
10	3	5	6	Not a urinary carrier		
11	19	49	56	20	56	63
14	19	49	56	Not a urinary carrier		
15	2	4	5	Not a urinary carrier		

The urine of three patients (cases 10, 14, and 15) recorded as not being urinary carriers on the results of preliminary investigation were not examined after treatment. The urine of case 9, who had not been found to be a urinary carrier in the preliminary investigation, was not examined after the end of treatment until the 131st day. The urine of case 5, who was still a fæcal carrier 10 days after the end of treatment, was not examined after the 95th day.

TABLE II—RESULTS OBTAINED WITH INTERMITTENT TREATMENT

(Sulphathiazole 100 g. and penicillin 57,600,000 units in 21 days)

Case no.	Isolation of *S. typhi*					
	Fæces			Urine		
	No. of specimens negative	Last day after end of treatment on which a negative result was obtained	First day after end of treatment on which a positive result was obtained	No. of specimens negative	Last day after end of treatment on which a negative result was obtained	First day after end of treatment on which a positive result was obtained
8	35	346	—	35	346	—
10	35	346	—	35	346	—
15	19	50	57	20	57	62

Specimens of both fæces and urine were examined on all occasions in the case of the patients treated by the intermittent method. Case 15, who, in the preliminary investigation, had not been found to be a urinary carrier, became one after treatment.

RESULTS

The results of the two trials are summarised in tables I and II.

It is doubtful how the result obtained with case 3 is to be classified. She died, 40 days after the end of treatment, from old-standing kidney disease. Cultures were made post mortem from bile, kidneys, spleen, small intestine, and bladder, all with negative results. These findings suggest that she was cured of the carrier condition, but owing to the inability of her kidneys to excrete penicillin rapidly the concentration of the antibiotic in her blood and hence in her tissues was enormously higher than would be attainable in a normal person. For this reason and because she did not survive for a year after treatment it is considered advisable to exclude her from further consideration. The patient whose treatment by the intermittent method had to be stopped, since it was considered to be prejudicially affecting her, has already been excluded. We have, therefore, remaining nine patients treated by the continuous method and three by the intermittent method.

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DISCUSSION

The criterion of cure of the carrier condition which we insisted on was stricter than most workers with experience of the bacteriology of typhoid fever would have demanded. It was far stricter than is required by any authority for the release of typhoid convalescents from the suspicion of being carriers. The cultural methods used were not only among those generally found most delicate and reliable for the isolation of *S. typhi* from fæces and urine but also were selected after test with the strains of the organism originally excreted by these carriers. That we were wise to demand a strict criterion is shown by the results obtained with cases 11, 14 and 15, from each of whom, during 7 weeks, 19 negative specimens of fæces were obtained, and yet in each case the subsequent specimen was positive. There is little doubt that, in the case of these patients, the treatment almost succeeded, and that only a very few bacilli survived, possibly in some relatively inaccessible position.

Even if success had not been achieved with other patients, one would be entitled to be encouraged by the results obtained in these three patients. The long period during which *S. typhi* could not be isolated from the fæces or urine of these patients warrants a review of the regulations at present in force regarding the examinations required before a suspected carrier is released. But, even if the examination of 20 specimens over a period of 2 months is to be insisted on, it is difficult to imagine the typhoid bacillus persisting, either in an inaccessible position or in a state of dormancy for a whole year in the bodies of patients 8, 9, and 10, who before treatment were excreting *S. typhi* in 6 out of 8, 7 out of 8, and 7 out of 8 specimens of fæces. It is, in general, almost impossible to prove a negative, and, in this particular case, to prove that a given person will not, some time in the future, begin to excrete typhoid bacilli. We claim that we have gone as near to proof as is practicable.

The remaining type of evidence to be considered is that afforded by the Vi agglutinin titres of the sera. It is generally agreed that there is a close, but not absolute, correlation between the presence of the organism in the body and of Vi agglutinins in the serum. An attack of typhoid fever, not followed by the development of the carrier condition, usually gives rise to non-persistent Vi agglutinin in the serum, whereas if the patient becomes a carrier the Vi agglutinin tends to persist. There is, so far as we know, no evidence about the Vi titres in persons who have been carriers for years and have then ceased to be carriers. The argument that, because a high proportion of Vi-positive persons can be shown to be carriers, every person whose serum agglutinates a Vi suspension of *S. typhi* at a dilution of, say, 1 : 20 or higher is a carrier, whether the organism can be found in his excreta or not, is invalid. It appears possible that long exposure of the tissues to Vi antigen will lead to a condition in which the antibody continues to be produced long after the stimulus has been withdrawn.

Before treatment was started, the Vi titres of the sera of the three patients whom we believe to have been cured were: case 8, 1 : 20; case 9, 1 : 5; and case 10, 1 : 80. The titres of the three, more than a year after the end of treatment, were: case 8, 1 : 20; case 9, negative at 1 : 5; and case 10, 1 : 25. For the reasons given above we do not consider that any great weight should be attached to these results.

After deliberate consideration of the whole question we conclude that we are justified in claiming that the treatment of ten chronic typhoid carriers has led to the cure of three of them. These figures are not very impressive, but it is doubtful if any other method of treatment has led to a cure of the carrier condition in 30% of cases. The patients selected for the test were rather elderly females who had been carriers for a long time and for the most part were in rather poor physical condition. Probably better results would have been obtained with persons who had been carriers for shorter periods.

Despite the smallness of the numbers, we believe that information of value may be adduced from a comparison of the results obtained by the two methods of treatment. Of the nine patients to be considered who were treated by the continuous method, one was cured, two were not excreting *S. typhi* during 49 days after treatment, and the remaining six began to excrete *S. typhi* again within 6, 11, 10, 12, 6, and 5 days. Of the three patients treated by the intermittent method, two were cured, and one did not begin to excrete the organism again until after 50 days.

Intermittent treatment was based on the occurrence of persisters, organisms which, being in a resting phase, are not susceptible to the action of penicillin. The success of the method appears to give support to the theory on which it was based. Its success in two out of the three patients treated by it is all the more impressive because these patients were not cured by the continuous method. It is believed that small modifications in the details of treatment, such as increasing the dosage of penicillin and increasing the number both of treatments and intermissions, would yield even better results.

It is suggested that the method, suitably modified, might be used in the case of convalescents to prevent the establishment of the carrier condition.

SUMMARY

Ten chronic typhoid carriers were treated with sulphathiazole 52 g. and penicillin 30,000,000 units given over a period of 6½ days.

One patient, who died of old-standing kidney disease 40 days after the end of treatment, is excluded from consideration. One patient, from whose fæces and urine *S. typhi* was not isolated in 35 examinations over 384 days, is regarded as cured. The remaining eight patients relapsed in 5–56 days after the end of treatment.

Three patients, in whom treatment had failed, were re-treated by the intermittent method using sulphathiazole 100 g. and penicillin 57,600,000 units in 21 days; four treatment periods, each of 3 days, being alternated with the rest periods of 2, 3, and 4 days. Two of the three patients treated by the intermittent method, from whose fæces and urine *S. typhi* was not isolated in 35 examinations over 346 days, are regarded as cured. The remaining patient began to excrete *S. typhi* in her fæces in 57 days, and in her urine in 62 days, after the end of treatment.

It is claimed that the method of treating the typhoid carrier condition here described is superior to any hitherto adequately tested, and that, with slight modifications, still further improvements might be obtained.

For the selection of patients and for their transfer to Dublin we are indebted to the medical officers of the Department of Health and particularly to Dr. J. A. Deeny and Dr. J. Kearney, to Dr. J. A. Stritch, bacteriologist to the City of Dublin, and to Drs. W. J. Coyne, D. L. Kelly, J. Fitzgerald, T. Foley, and D. J. Courtney, the resident medical superintendents of the mental hospitals from which the patients were drawn. We are also grateful to these gentlemen for supplying us with specimens from treated patients after their return. We are particularly grateful to Dr. John Dunne for all he did in connexion with the reception and treatment of the patients in Grangegorman Mental Hospital and to Dr. D. J. O'Sullivan under whose clinical care the patients were during treatment. Without her skill and reliability the investigation could not have succeeded. We are indebted to Dr. A. Felix, F.R.S., for having typed the strains of *S. typhi* isolated, and for having determined the Vi titres of the sera of cured patients. We thank our colleagues in the department of bacteriology in Trinity College for their assistance and particularly Dr. J. D. McKeever, who was responsible for the examination of

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specimens in the later stages of the investigation. Messrs. Glaxo Laboratories Ltd. supplied the penicillin.

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MATERNAL RUBELLA AND CONGENITAL DEFECTS

DATA FROM NATIONAL HEALTH INSURANCE RECORDS

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SINCE the original observations of the Australian workers on the association between rubella in the pregnant woman and the occurrence of congenital defects in the child, many similar, but rather haphazardly observed, cases have been reported from the U.S.A., Great Britain, and elsewhere. That evidence, which we need not review here, seems to us sufficiently strong to substantiate the association—i.e., that rubella early in pregnancy can cause defects in the fœtus. What we regard as still undetermined with any accuracy is the frequency with which the disease will lead to abnormalities.

From the evidence then available Swan et al.[1] concluded that rubella contracted within the first two months of pregnancy would almost invariably lead to a defective child, whereas in the third month the chance might be about 50%. Many of these, and other, important original observations were, however, made retrospectively—by noting the congenital deformity in the newborn child and then obtaining the history of the mother during pregnancy. By such a method it is clearly impossible to obtain the required probabilities of a defect arising. To take a simple example, 20 women might have rubella in the first two months of pregnancy and 10 give birth to defective children. The true, required, probability is 50%. On the other hand, if we work retrospectively solely from the 10 defective children we should automatically reach a 100% association—all their mothers had rubella. In other words, a fundamental requirement for the measurement of the risks involved is a forward mode of inquiry. The attack of rubella must first be observed in the pregnant woman; the condition of the child born to her must subsequently be noted.

Such an inquiry is extremely difficult to carry out, for very large numbers of women must be observed, and it is specially important that the occurrence of the disease in them be recorded at a time when they may not even know that they are pregnant. These difficulties are clearly apparent in an investigation made this way by Fox and Bortin[2] in Michigan, where out of some 22,200 notified cases of rubella in 1942–44 these workers could finally detect and trace only 11 women who were pregnant at the time of their illness.

A similar inquiry by Ober et al.[3] gave results on a larger scale. Starting from some 35,000 notified cases of rubella in Massachusetts in 1943, they identified from the notification returns 3068 women aged 17–49. Approaching these women by mail they collected 49 instances of rubella during pregnancy, and to these they added another 5 discovered by other methods. Less than half the women approached, however, chose to reply to the letter. Hence it is not known whether the cases finally discovered are a representative group of all such cases. The probabilities might well be affected in this way; but, the sample being accepted as it stands, the results show that of 5 women who had rubella during the first month of pregnancy 2 aborted, 2 had defective infants, and only 1 had a normal infant. In the second-month attacks 2 infants were stillborn, 2 were defective, and 4 were normal. In the third-month attacks 2 mothers aborted, 1 child was defective, and 6 children were normal. In the later attacks, from the fourth to the ninth month, there were 25 normal infants, only 2 doubtful defects, and 3 losses by abortion or stillbirth.

Clearly one of the main difficulties is to secure sufficient cases for investigation without a prohibitive amount of work. An additional difficulty in this country is that rubella is not notifiable (Manchester, we believe, is the only exception to this rule). It is therefore impossible to follow the examples cited above from the U.S.A. and to collect cases from notifications of infectious disease. The method of observing carefully all women attending prenatal clinics is not likely to be of much help, since the women do not attend the clinics often enough for this purpose during the early weeks of pregnancy. Some other method of case-finding must therefore be found.

PRESENT METHOD OF INQUIRY

It occurred to us that one way of securing records of rubella in pregnancy and the birth of a child was to use the data collected by the approved societies operating under the National Health Insurance Acts before July 5, 1948. If an employed and insured married woman drew benefit for a sickness which caused her to be absent from work she had to present a sickness certificate giving the precise dates of her illness and the general practitioner's diagnosis. If she subsequently gave birth to a child she would be entitled to draw maternity benefit, and the date of the birth would also be recorded. Thus whether she was in the first month of pregnancy and unaware of it, or in the ninth and under no illusions, the occurrence and the dates of the two events would be recorded.

The drawbacks were that: (1) we were necessarily limited to employed insured women and might therefore not get enough cases; (2) we should observe only cases of rubella severe enough to cause absence from work; and (3) we should have to rely on the general practitioner's diagnosis. Perhaps (2) and (3) to some extent cancel one another, leaving us with only the more clear-cut cases to work on and freeing us from dealing with fleeting and doubtful rashes.

We concluded that this method of approach was at least worth a trial, for it was simple to operate and would lend itself to the observation also of other diseases than rubella during pregnancy. That is clearly an important point, since the evidence concerning the possible effects on the fœtus of other infectious diseases in pregnancy—e.g., measles and mumps—is at present both scanty and unconvincing. We therefore asked some large approved societies to take special note of all cases of rubella and measles in married women, and to observe whether any of these women gave birth to a child within 12 months of the end date of the recorded illness. For these "double-event" cases they filled in a "notification" form and returned it to us. We made the post-illness interval 12 months for ease of operation and because we thought that some of the immediate preconception illnesses might be of interest. No controls were needed, because our sole interest lay in the relative

* Holding a Rockefeller Foundation fellowship in preventive medicine.

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attack-rates of congenital defects that followed rubella or measles contracted at different times during pregnancy, and because we were mainly testing a method of inquiry and not expecting to get enough material to answer problems. In this last conjecture we were certainly not at fault, for in about two years we have had only 22 notifications.

FOLLOW-UP

The next step was to examine the babies. For this purpose, after communicating with the mother's doctor, one of us (T. McL. G.) visited all the mothers except 2, who were not traced. Probably with extra effort we could have traced these, but both had had measles almost a year before the birth of the child, and so we did not regard them as important.

A full history of the pregnancy and a family history were taken. The mother's illness was particularly inquired into to determine whether there appeared to be any doubt about the diagnosis. Except 2 babies who had died and 1 living infant (case 16), all the children were given a full clinical examination. Permission to examine case 16 was refused, but the mother insisted that the child was normal in every respect. Attention was particularly directed to the heart, eyes, and ears, but a complete search was made for abnormalities elsewhere.

As regards the diagnosis we have doubts over 4 cases:

Case 18 was originally reported as a case of measles. The mother said she had been off work with morning sickness when she was reported to have measles. She had asked her doctor not to put morning sickness on her certificate, so that her workmates might not know of her pregnancy. Possibly a somewhat illegible "morning sickness," or "emesis," had subsequently been deciphered as "measles."

The illness of case 19 had been regarded as chickenpox both by the patient and her doctor, and it appears to have been notified to us as a case of measles by mistake.

In case 20 subsequent recurrences of the syndrome originally notified as measles had caused the doctor to revise his diagnosis to one of occupational dermatitis.

The only case of more serious import was case 12, where the original diagnosis was rubella occurring early in the first month—i.e., one of the important cases. The mother, in spite of her doctor's diagnosis, maintained that she had had measles and not german measles. Strongly supporting her

TABLE I—PREGNANT WOMEN WITH RUBELLA

Case no.	Age of mother at confinement (yr.)	Recorded date(s) of illness	Date of confinement	Estimated time of occurrence of illness in pregnancy	Clinical findings in child
1	23	March 17 to 26, 1947	Nov. 26, 1947	End of first month	Congenital heart disease (patent interventricular septum)
2	24	June 13 to 21, 1947	Feb. 11, 1948	Middle of second month	(Died aged 5 weeks; certified cause of death, pneumonia)
3	22	May 14 to 21, 1947	Dec. 4, 1947	Third month	No abnormality detected
4	26	April 9, 1947	Oct. 21, 1947	" "	" "
5	21	April 15 to 22, 1947	Oct. 30, 1947	" "	" "
6	21	April 26 to May 3, 1947	Oct. 26, 1947	Fourth month	" "
7	21	April 7 to 15, 1947	Sept. 18, 1947	" "	" "
8	23	July 1 to 16, 1946	Nov. 12, 1946	Sixth month	(Died aged 7 days; certified cause of death, pneumonia)
9	25	Aug. 3 to 10, 1946	Oct. 10, 1946	Eighth month	No abnormality detected
10	23	April 19 to 26, 1947	Feb. 23, 1948	A month before conception	" "

TABLE II—PREGNANT WOMEN WITH MEASLES

11	25	April 18 to May 10, 1947	Jan. 29, 1948	? Pre-conception ? Early in first month	No abnormality detected
12	20	April 8, 1947	Jan. 7, 1948	Early in first month	" "
13	26	Dec. 23, 1946	June 16, 1947	Fourth month	" "
14	26	June 21 to July 13, 1946	Nov. 18, 1946	Fifth month	" "
15	21	March 27 to April 12, 1947	July 5, 1947	Seventh month	" "
16	25	Jan. 31 to Feb. 14, 1947	March 3, 1947	Ninth month	(Permission to examine child refused. Reported normal in all aspects)

TABLE III—MISCELLANEOUS GROUP

Case no.	Age of mother at confinement (yr.)	Illness notified	Illness which occurred	Date(s) of illness	Date of confinement	Estimated time of occurrence of illness in pregnancy	Clinical findings in child
17	26	Rubella Infective hepatitis	Rubella Infective hepatitis	April 26 to May 16, 1946 Oct. 26 to Dec. 10, 1946	March 4, 1947	Pre-conception (one month) Sixth month	No abnormality detected
18	27	Measles	Morning sickness	June 17 to 29, 1946	Feb. 15, 1947	Second month	" "
19	19	Measles	Chickenpox	April 21 to May 17, 1947	Sept. 27, 1947	Fifth month	" "
20	22	Measles	Occupational dermatitis	Dec. 2 to 7, 1946	Aug. 17, 1947	First month	" "
21	32	Measles	—	May 10, 1946	May 28, 1947	Pre-conception (three months)	Not traced
22	31	Measles	—	May 23 to June 29, 1946	May 14, 1947	Pre-conception (two months)	" "

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belief was her statement that about a fortnight after the onset of her own illness other members of the family had fallen ill with what had been diagnosed by the doctor as measles. Further weight is perhaps given to her belief by the fact that the baby, born nearly nine months later, developed rubella at the age of 5 months. In this history we have, after some hesitation, revised the diagnosis from rubella to measles. The case is clearly important, for the illness was in the first month of pregnancy and the child was unaffected—a point which, of course, we must not allow to influence our decision.

RESULTS

The protocols of these 22 cases are presented briefly in tables I–III and call for an equally brief discussion.

From table I it will be seen that there were 10 cases of rubella. In case 1 we estimate that the attack was in the first month of pregnancy, and the resulting child was congenitally defective—the only affected child we found. It had congenital heart disease—a patent interventricular septum. No abnormality of the eyes or ears was detected. In case 2 the attack of rubella was probably in the middle of the second month; unfortunately the child had died at the age of 5 weeks, the certified cause being pneumonia. In cases 3, 4, and 5 we place the attack of rubella in the third month of pregnancy, and not one of these infants showed any abnormality. The attacks of rubella which occurred later in pregnancy were not associated with congenital defects, but in case 8 the infant had died at the age of 7 days, pneumonia again being the certified cause of death.

Table II shows 6 cases of measles which occurred in the first, fourth, fifth, seventh, and ninth month of pregnancy. No abnormalities whatever were found in association with them.

Table III shows 6 miscellaneous events. Cases 18 to 22 have already been referred to above and need no further discussion beyond the observation that an attack of chickenpox in the fifth month had no effect on the fœtus. Case 17 is included as a case of rubella about a month before conception, followed by infective hepatitis in the sixth month. Neither event had any observed effect on the infant.

DISCUSSION

As we have already pointed out, this inquiry has produced far too little information to give even the most tentative of answers to our original problem: what is the probability of congenital malformations in a child resulting from rubella in the mother at different stages of her pregnancy? We can but add some few more observations to those already existing and, perhaps, particularly note that with rubella in the third month all 3 babies were normal. As regards measles, we may note that one attack, and possibly two, occurring in the first month of pregnancy led to no defects in the babies. In other words, with measles even its earliest occurrence in pregnancy does not necessarily (if at all) carry a risk of congenital abnormality.

Our main interest, however, lay in the approach to the problem, and we believe, considering our very limited field of inquiry, that the method has distinct possibilities. The recording of the "double event" has, we believe, presented no great difficulty to the approved societies that assisted us. The diagnosis clearly raises problems, but on the whole we believe that the evidence we finally collected in relation to the original diagnosis is as good as can be obtained in this field. If the rubella case were to be immediately visited when the sickness was in being, for a special clinical examination, that procedure would involve visiting many non-pregnant women and probably make the system impossible. It is essential to await the birth of a child. Very shortly after that birth, however, a visit should be paid lest, as in 2 of our cases, the child should die. At that time all the congenital abnormalities might not be apparent, and a subsequent visit, or even visits, would be necessary. In exploring the method we deliberately risked losses by death and delayed the visits. Other infectious diseases, or any non-infectious diseases likely to cause absence from work, could easily be included in a more extended inquiry. We hope, therefore, it may be possible to extend these observations through the records of the new health and social services.

SUMMARY

By means of records collected by approved societies operating the National Health Insurance Acts (before July 5, 1948), it has been possible to detect and trace women who had an infectious disease within the period of pregnancy and to observe the effects on the child subsequently born.

This method, if used widely under the new health and social services, might in a few years provide an answer to the important question: what is the probability of congenital malformations occurring in a child as a result of an illness in the mother at different stages of her pregnancy?

We are sincerely grateful to the approved societies who recorded and notified these cases to us in confidence and thereby made the inquiry possible; to the practitioners who gave us much help and allowed their patients to be visited; to the mothers for their forbearance and coöperation; and to the Medical Research Council, who defrayed the expenses incurred in visiting the mothers.

CONGENITAL ABSENCE OF THE GALL-BLADDER

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DEVELOPMENTAL abnormalities of the gall-bladder occasionally give rise to difficulty in diagnosis and in surgical treatment. They include double gall-bladder, diverticulum of the gall-bladder, floating gall-bladder, hour-glass gall-bladder, and abnormally placed gall-bladder (left-sided; retro-displacement; intrahepatic; transverse displacement). In the case reported below neither a gall-bladder nor a cystic duct could be found at operation.

Congenital absence of the gall-bladder is generally regarded as a very rare anomaly in man. Some doubt, indeed, whether the condition occurs at all, except in association with gross malformation or congenital absence of the main bile-ducts: they hold that, if the main bile-ducts are intact and pervious, a gall-bladder must also be present, though probably situated in some abnormal position overlooked by the surgeon.

It must be granted that in most cases of congenital absence of the gall-bladder there is gross malformation or agenesis of the extrahepatic ducts; and the large majority of children with this condition die in the first 3–6 months of life, the greatest age attained in the series collected by Stolkind (1939) being 15 months. In such cases jaundice is present at birth or develops in the first 3 weeks, the stools being clay-coloured from the beginning. The fact that a child may be born without a gall-bladder yet grow to adult life has been proved conclusively at necropsy, notably in two cases from the London Hospital (Prof. H. M. Turnbull) and Guy's Hospital (Prof. Payling Wright); where the patients were both men over 50 years of age.

Aristotle knew that man can be born without a gall-bladder and live, and he recognised also that the horse, mule, ass, deer, camel, dolphin, and sea-calf, are born without gall-bladders. To this list Pliny added the wild boar, and Haller

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the elephant, ostrich, peacock, parrot, and cuckoo. According to Devine (1942) herbivora crop their food and have a means of converting a discontinuous to a continuous food-supply, whereas carnivorous animals feed at irregular intervals on food containing a large quantity of fat, which requires large quantities of bile at a time to emulsify the food. In general it may be said that carnivora are born with gall-bladders whereas herbivora often have none.

Notwithstanding the emphasis laid on its rarity, congenital absence of the gall-bladder is commoner than is thought. As Finney and Owen (1942) observed, "many surgeons come upon very remarkable and rare cases but the information concerning these never gets beyond their office files." Gross (1936) collected 38 cases in which the gall-bladder and cystic duct were absent, the hepatic and other ducts being present and functioning. To this list Finney and Owen (1942) added 10 more cases, making a total of 48, including 2 of their own. They drew attention to the fact that many of the reports were notably lacking in essential data. In 11 cases where the reports were complete they noted that all the patients had calculi in the common duct and in all but 1 the duct was dilated. These workers were evidently unaware of the large series of cases collected by Stolkind (1939) from London hospitals. In 246 cases of abnormalities of the gall-bladder he reported 31 cases of absence of the gall-bladder. He considered that congenital absence of the gall-bladder could be proved only by necropsy, since diagnosis at operation, or by radiography, or both, was insufficient proof. If one accepts this opinion, many of the reported cases would be ruled out. Today, however, we have at our disposal a further and useful method of investigation—cholangiography—of which use may be made after operation to confirm or disprove the diagnosis made at operation. This investigation was carried out in the case reported below.

Two theories have been advanced to explain the absence of the gall-bladder:

(1) In the fœtus a diverticulum develops from the fore-gut to form the liver and the extrahepatic ducts. The gall-bladder and cystic ducts develop from this diverticulum as an out-pocket. Failure of such development would cause complete absence of the gall-bladder and cystic duct—a simple if ingenuous explanation.

(2) The hepatic, common, and cystic ducts, as well as the gall-bladder, are at first hollow structures. Later their lumen is obliterated during the solid phase through which all these structures pass. Still later it is re-established and the normal channels are formed. This final stage may be arrested in any portion of the biliary tract, with resulting atresia of the part affected.

Congenital absence of the gall-bladder seems to be twice as common in females as in males, and at operation the fossa of the gall-bladder is usually absent, or occasionally a fissure is found on the under surface of the right lobe. The quadrate lobe is usually poorly defined or absent.

FUNCTIONS OF THE GALL-BLADDER

The normal healthy gall-bladder in man has a capacity of $1^1/_2$–3 oz. and it not only acts as a reservoir but also reduces the bile to a concentration ten times that of the bile formed in the liver. The liver secretes about a pint of bile in a day,* and concentration in the gall-bladder is brought about chiefly by absorption of water and salts. In addition the gall-bladder secretes mucus, estimated at about 20 ml. in 24 hours, and regulates the pressure in the bile-ducts. It is stimulated to contract by a hormone (cholecystokinin) generated in the duodenum and upper part of the small intestine. Ivy (1934) states that the most effective excitants of the production of this hormone are acids and fats. All fats are effective, particularly egg-yolk and cream, and the hormone is generated irrespective of anatomical alteration produced by such operations as gastro-jejunostomy or gastrectomy. Contraction of the gall-bladder is said to be accompanied by relaxation of the sphincter of Oddi, though some physiologists do not accept this theory. In any event the concentrated bile or, as Pavlov called it, "ignition" bile is forced into the duodenum by contraction of the gall-bladder in response to stimulation by the hormone.

CLINICAL FEATURES

In published cases of complete absence of the gall-bladder the patients have come to operation for the usual symptoms of cholelithiasis and commonly complain of flatulent indigestion; sharp piercing pain in the epigastrium and right upper quadrant of the abdomen, reaching back to the right scapula; intolerance of fatty foods; and, in some cases, attacks of jaundice. Cholecystography reveals complete lack of filling of the gall-bladder, which merely leads to the diagnosis of diseased gall-bladder. (It is worthy of note that gall-stones have been found in animals, even in those not possessing a gall-bladder, such as the horse and ox.)

If at laparotomy for suspected gall-bladder disease a gall-bladder is not found in the normal position beneath the right lobe of the liver, careful search should be made for a gall-bladder in any of the recognised abnormal positions for that organ. A left-sided gall-bladder, which may be present without transposition of viscera, should not cause any difficulty. A transversely placed gall-bladder lying in the hilum of the liver will be harder to remove but should be found with comparative ease. The most perplexing and dangerous cases are those of retro-displaced and of intrahepatic gall-bladders.

The retro-displaced gall-bladder lies in the inferoposterior portion of the liver. It is usually invisible and may lie retroperitoneally along the inferior vena cava, where its presence can be demonstrated only by palpation, and drainage or removal of stones presents serious difficulties.

An intrahepatic gall-bladder may be completely or only partially embedded in the liver. If it is completely embedded, a prominence on the anterior surface of the right lobe may indicate its situation. Partial exposure—e.g., of the tip of the fundus, and of a portion of the neck—will also serve as a guide. The gall-bladder has been found at a distance of 3–4 cm. from the surface, with no cystic duct seen outside the liver (Walter and Neiman 1931). Mauro (1940) warns against the danger of attempting to remove such a deeply embedded gall-bladder, since this may lead to severe hæmorrhage and shock. It is significant that all the intrahepatic gall-bladders reported have contained stones. Such cases are better treated by incision, removal of the stones, and drainage, supplemented by cauterisation of the mucosa if deemed wise or necessary.

Griffiths (1944) makes an almost casual reference to a most interesting case:

> "X-ray examination showed several moderate sized stones tightly packed together; at operation he found the gall-bladder in the usual site with one small stone in the neck. As this finding did not fit in with the X-ray report further examination of the right lobe disclosed a slight bulge lateral to the fossa of the gall-bladder. The liver was incised over the prominence and a spherical gall-bladder packed with stones was disclosed. The gall-bladder shelled out easily and was removed. The duct leading from it suggested that it was on its way to join the right hepatic duct in the fissure."

If the aforesaid malpositions are not found and, after the common bile-duct and its tributaries have been traced into the hilum of the liver, there is no sign of a gall-bladder, even vestigial, congenital absence of the gall-bladder may be diagnosed, in which case there will probably be a stone or stones in the common bile-duct, which should be opened and drained after removal of all calculi. In

* In 87 cases of common-duct drainage by T-tube, I found the lowest recorded drainage of bile in 24 hours was $10^1/_2$ oz. and the highest 24 oz. In the latter case drainage was into a bottle attached to the bedside. In common-duct drainage the bottle—preferably a baby's bottle—should be attached to the binder or dressings, and so placed that its horizontal level is not lower than that of the common duct. Otherwise all the bile will tend to pass by gravity into the bottle.

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(a) (b)

Cholangiograms 12 days after operation: (a), showing dilated bile-ducts but no gall-bladder; (b), after hypodermic injection of morphine gr. 1/4, showing fuller outline of bile-ducts due to stimulation of Oddi's sphincter by morphine.

the case recorded below full investigations were carried out and the absence of the gall-bladder was demonstrated by cholangiography.

CASE-RECORD

A woman, aged 72, was first seen at hospital on Sept. 21, 1943. She had enjoyed excellent health until November, 1940, when she began to have attacks of epigastric pain which moved across the right hypochondrium and back to the right scapula. The pain was very severe—she had to go to bed for several hours—and made her feel weak and perspire heavily. The attacks, which were not related to food, came on at first at two-month intervals until autumn, 1941, when jaundice appeared. The jaundice fluctuated but never disappeared, and the attacks of colic became more frequent, occurring every three weeks.

The patient attended the outpatient department of the Wilson Hospital, Mitcham, on Sept. 21, 1943, when jaundice was pronounced. A plain radiogram did not show any radio-opaque shadows in the gall-bladder region. Chronic cholecystitis and subsequent jaundice from stone in the common bile-duct was diagnosed.

Laparotomy (Oct. 5, 1943).—At operation the gall-bladder was not found. The fossa for the gall-bladder was absent, and the recognised abnormal sites for the gall-bladder were explored without result, but a large stone was palpated in the common duct, which appeared to be much dilated. The stone was removed, no further stones were found, the duct was cleared of debris by suction and syringing with saline solution, and drainage of the common duct was established with a T-tube.

Cholangiography.—Twelve days after operation the bile-ducts were outlined with an opaque medium ('Neo-hydriol') introduced through the T-tube. The first picture showed dilatation of the ducts but no evidence of gall-bladder or filling defect due to stone (see figure (*a*)). A second radiogram, taken after the hypodermic injection of morphine gr. 1/4, showed the stimulating effect of morphine on the sphincter of Oddi, causing strong contraction and thus helping to outline the bile-ducts to the full extent (see figure (*b*)).

The T-tube was kept in position until the bile was free from pathogenic bacteria, cholesterol crystals, biliary sand, and the percentage of bile salts was within normal limits.

The patient made a good recovery, and a message from her medical attendant (Dr. David Millar, of Mitcham, Surrey) in July, 1948, stated that she had had no further recurrence of biliary trouble, but had secondary anæmia.

Dr. Cuthbert Dukes reported on the stone as follows: "The specimen consisted of an oval light-reddish brown stone measuring 3/4 in. in its longest axis and weighing 2 g. It was soft and crumbly. Small fragments both from the outer shell and from the inner and rather harder central core were removed and pulverised for chemical analysis. On heating, the powder burnt with a smoky luminous flame with an odour of burning fat. Only a very small residue was left. Extraction with chloroform showed the presence of about 60% of soluble material, which consisted chiefly of cholesterol. This was confirmed both by chemical test and microscopical examination. Bile pigments composed most of the remainder of the stone, only small traces of inorganic salts being found."

CONCLUSIONS

A gall-bladder is not essential to the newborn. What is essential is that the main extrahepatic ducts should be present and pervious, with a free opening into the duodenum.

There is no distinctive feature by which congenital absence of the gall-bladder can be diagnosed before operation. Cases that have been discovered at operation have come to the surgeon because of the clinical features associated with stone or stones in the common bile-duct. It should be noted, however, that not all these patients have jaundice. This is in keeping with the findings of Lahey (1938), Cattel, and others that jaundice is not necessarily a corollary of stone in the common duct, at least 35% of cases not showing this feature.

Gall-stones can be formed irrespective of the presence or absence of a gall-bladder. In horse and ox, which do not possess a gall-bladder, stones have been found in the biliary tract. All intrahepatic gall-bladders reported have contained stones.

It is commonly held that, when the gall-bladder is removed, the bile-ducts dilate and take over in part the functions of the gall-bladder, but it has been noted in some cases of congenital absence of the gall-bladder that the ducts are not abnormally dilated. In fact some believe that the bile-ducts do not become dilated unless stone or stones are a complication. In their opinion congenital absence of the gall-bladder, or removal of the organ by operation, leads to a compensatory relaxation of the sphincter rather than dilatation of the common bile-duct.

So far as can be ascertained, the case reported here is the first in which cholangiography has been used to confirm the operation diagnosis of congenital absence of the gall-bladder.

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MULTIPLE PREGNANCIES AND ERYTHROBLASTOSIS FŒTALIS

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VARIOUS explanations have been given of the discrepancy between the incidence of erythroblastosis fœtalis and that of Rh-incompatible marriages. The heterozygosity of Rh-positive husbands does explain this discrepancy, since the incidence of Rh-incompatible marriages is about 13% (Wiener 1943), whereas that of erythroblastosis fœtalis is only 0·1–0·2% (Buxton and McDuff 1945). Insufficient maternal immunisation as a result of the limitation of pregnancies has been one of the most generally accepted explanations. Thus, according to the original theory of Levine, only the second or third pregnancy in Rh-incompatible marriages can sufficiently immunise the mother to produce erythroblastosis fœtalis or hæmolytic disease of the newborn. Cappell (1944) observes that hæmolytic disease of the newborn may first appear after ten or more normal children have been born.

To test this explanation we studied a group of Rh-negative women who had married Rh-positive men and had had a considerable number of pregnancies. The incidence of Rh-negative women among our obstetrical material is 9·6%, and the incidence of erythroblastosis fœtalis 0·05% (Gurevitch et al. 1947). The incidence of

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erythroblastosis fœtalis among Rh-negative women is 0·5%.

We selected 32 Rh-negative women who were married to Rh-positive men and had had 6–14 pregnancies and at least 6 deliveries at term. Their blood was repeatedly examined for agglutinating, blocking, and conglutinating Rh antibodies* before, during, and after the last pregnancy, and in some cases before, during, and after the last two pregnancies. A group of 34 Rh-positive women who had 6–14 pregnancies were used as controls.

RESULTS

The results of pregnancies and deliveries in the Rh-negative group are given in table I. No antibodies were found. These women had had 311 pregnancies, which had ended in 268 normal deliveries at term, 7 premature deliveries (1 stillbirth), 30 miscarriages, 5 stillbirths, and 1 artificial abortion. The stillbirths were all due to obstetric conditions (toxæmia of pregnancy, premature separation of placenta, prolapse of the umbilical cord, &c.). In none of the stillbirths were any signs of hæmolytic disease found, such as hydrops fœtalis or kernicterus. Of the children born alive none developed erythroblastosis or any other form of hæmolytic disease of the newborn. All the children were carefully examined, and blood-counts and typing were done in most cases. The analyses of pregnancies and deliveries (premature deliveries, miscarriages, and stillbirths) in the Rh-negative (table I) and the Rh-positive groups (table II) were not significantly different.

* The tests were performed according to the technique described by Wiener (1945).

TABLE I—TERMINATION OF PREGNANCY IN 32 RH-NEGATIVE WOMEN MARRIED TO RH-POSITIVE MEN

Case no.	No. of pregnancy														Total normal deliveries at term
	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th	13th	14th	
1	N	N	N	Sp. ab.	N	N	N	..	..	..	..	..	..	..	6
2	Art. ab.	N	N	N	N	N	N	..	..	..	..	..	..	..	6
3	N	N	N	N	N	Sp. ab.	N	..	..	..	..	..	..	..	6
4	N	N	N	N	N	N	N	..	..	..	..	..	..	..	7
5	N	N	Sp. ab.	N	N	N	N	..	..	..	..	..	..	..	6
6	Sp. ab.	N	N	N	N	N	N	..	..	..	..	..	..	..	6
7	N	Sp. ab.	N	N	N	N	N	N	..	..	..	..	..	..	7
8	N	N Twins	N	N	Sp. ab.	Pr.	N	N	..	..	..	..	..	..	6
9	N	N	N	Sp. ab.	Sp. ab.	N	N	N	..	..	..	..	..	..	6
10	N	N	N	N	N	N	N	N	..	..	..	..	..	..	8
11	N	N	N	N	N	N	N	N	..	..	..	..	..	..	8
12	N	N	N	N	N	N	N	N	N	..	..	..	..	..	9
13	N	N	Sp. ab.	N	N	N	N	N	N	..	..	..	..	..	8
14	N	N	N	Pr.	N	N	N	N	N	..	..	..	..	..	8
15	N	N	N	N	N	Sp. ab.	N	N	N	N	..	..	..	..	9
16	N	N	N	N	N	N	N	Sp. ab.	N	N	..	..	..	..	9
17	N	N	N	Pr. stil.	N	N	Sp. ab.	N	N	N	..	..	..	..	8
18	N	N	N	Sp. ab.	Sp. ab.	Sp. ab.	N	N	N	N	..	..	..	..	7
19	N	N	N	N	N	N	N	N	N	N	..	..	..	..	10
20	N	Sp. ab.	N	N	N	Pr.	N	N	N	N	..	..	..	..	8
21	Pr.	N	N	N	N	N	N	N	N	N	..	..	..	..	9
22	Stillbirth	N	N	N	N	Sp. ab.	N	N	N	N	N	..	..	..	9
23	Sp. ab.	Sp. ab.	N	N	N	Sp. ab.	N	N	N	N	Stillbirth Cæs. sect.	..	..	..	7
24	N	N	Pr.	N	N	N	N	N	N Twins	N	N	..	..	..	10
25	Sp. ab.	Still-birth	N	N	N	N	N	N	N	N	N	..	..	..	9
26	N	N	N	N	N	N	N	Stillbirth	N	N	N	..	..	..	10
27	N	N	N	N	N	N	N	N	Sp. ab.	N	N	N	..	..	11
28	N	N	N	N	N	N	N	N	N	N	N	N	..	..	12
29	N	N	N	N	N	N	N	N	Sp. ab.	Sp. ab.	Sp. ab.	N	..	..	9
30	N	N	N	N	N	Sp. ab.	Sp. ab.	N	N	N	N	N	N	..	11
31	Pr.	N	N	N	Sp. ab.	N	N	N	N	Sp. ab.	N	N	N	N	11
32	N	N	N	N	Stillbirth	N	N	Sp. ab.	N	N	N	N	N	N	12
Total	..	..	..	..	..	..	..	..	..	..	..	..	..	..	268

N	= Normal delivery at term	268	(86·1%)
Sp. ab.	= Spontaneous abortions	30	(9·6%)
Art. ab.	= Artificial abortions	1	(0·3%)
Stillbirth		5	(1·5%)
Pr.	= Premature delivery	7	(2·2%)
	Total	311	

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TABLE II—TERMINATION OF PREGNANCY IN 34 RH-POSITIVE WOMEN

Normal delivery at term	Premature delivery	Stillbirths	Miscarriages	Total
276 (85·1%)	9 (2·8%)	4 (1·5%)	35 (10·7%)	324

DISCUSSION

Several views are held about the way in which the fœtal Rh-positive erythrocytes gain access to the maternal circulation. Levine et al. (1941) hold that this follows damage to the placenta; whereas Wiener and Sonn (1946) hold that it happens near or during labour. According to both these views the passage of incompatible fœtal antigen is presumed to have taken place in the cases reported. However, a most striking feature of our cases is the absence of any signs of maternal immunisation or of fœtal damage as a result of repeated Rh-incompatible pregnancies. Wiener and Sonn (1946) have suggested that this is due to a constitutional factor which confers the ability to produce antibodies in response to an incompatible antigen. On the other hand, those of our Rh-negative women who bore erythroblastotic children did so in their second or third pregnancies.

CONCLUSION

From a study of 32 Rh-negative women married to Rh-positive husbands the conclusion may be drawn that repeated incompatible pregnancies (6–14) are in themselves insufficient to cause maternal immunisation. This seems to invalidate the view that hæmolytic disease of the newborn is a relatively rare condition because of the limitation of the number of pregnancies in Rh-negative women married to Rh-positive men.

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LYMPHOSARCOMA PRESENTING AS ŒDEMA OF THE EYELIDS

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SECONDARY involvement of skin in cases of lymphosarcoma is not uncommon: it was noted in 22% of 618 cases of malignant lymphoma collected by Gall and Mallory (1942). But lymphosarcoma presenting as a skin lesion is very rare.

CLINICAL RECORD

On May 19, 1947, a married woman, aged 61, was admitted to St. Thomas's Hospital with a swelling round the left eye. Her husband had noticed it first two weeks previously, since when it had slowly enlarged. There was no pain, tenderness, or irritation, and the patient thought it was due to an insect bite, aggravated by bathing with too hot boracic lotion. There were no general symptoms, headaches, or visual disturbances, though the left eye had been sticky on waking. Previous history negative.

Examination showed a soft swelling and redness of the skin for about 1 in. round the left eye, with subcutaneous induration but no involvement of bone. General examination revealed nothing abnormal apart from a few isolated lipomata. Temperature, blood-counts, and radiography of chest normal. The left frontal and maxillary sinuses were slightly opaque to X rays, but this was attributed to overlying tissue. No bony disease of sphenoids or base of skull was found.

Treatment and Progress.—Facial cellulitis was tentatively diagnosed, and patient was treated with penicillin and sulphadiazine. But the swelling continued to enlarge, the skin becoming more congested, and there was some chemosis. On May 25 the palpebral fissure was completely closed, and it was impossible to part lids, both of which were very œdematous (fig. 1). Also there was induration at the edge of the lesion, which was extending across the bridge of the nose; it was purplish and suggestive of peau d'orange. The left eye, the nose, and nasopharynx were not diseased and no bruit was heard over the left face.

Since there was no response to penicillin, angioneurotic œdema was considered and 'Benadryl' was given, with no relief. A course of anodal galvanism, begun on June 3, brought considerable improvement: after a week, the swelling was reduced and less tense, and the patient could open her eye. She was discharged home on June 10.

On June 14 she had a sudden attack of nausea and brought up some blood. Four days later she again felt sick and vomited her breakfast, the vomitus being tinged with blood. A few hours later she felt ill and lost much blood from her nose.

Fig. 1—Lymphosarcoma presenting as œdema of eyelids.

Final Illness.—Readmitted on June 26, she had severe anæmia: Hb 38%, red cells 2,500,000 per c.mm., white cells 7650 per c.mm. (polymorphs 76%, eosinophils 3%, lymphocytes 12%, monocytes 9%). The lesion round left eye had extended across nose, though œdema of the lids had disappeared. The lesion appeared to be confined to skin. General examination revealed nothing else abnormal, and the patient was transfused with two pints of blood.

June 29: general condition much improved, but pain in both shoulders and weakness of left hand. All intrinsic muscles of left hand wasted, with weakness of wrist flexion and elbow extension. Flexor pollicis brevis weak on right side. No sensory change or other abnormality in central nervous system. Barium meal, and radiography of chest and cervical spine, showed no sign of disease. Cerebrospinal fluid normal.

July 4: a biopsy specimen (fig. 2) was taken from indurated skin on lateral margin of left orbit. Within a week the swelling had disappeared and no infiltration of skin could be felt. Biopsy report suggested lymphosarcoma.

July 16: hard nodule below and lateral to right orbit; side of the face still soft and pliable. Nodule grew rapidly in next few days.

July 20: gross œdema of left leg. Nodule on the face treated with X rays and disappeared completely within 10 days. Œdema of left leg diminished slowly during next fortnight, and patient was then allowed up. For ten days her condition was excellent: no signs of recurrence in the face, no deposits elsewhere; leg practically normal.

On Aug. 14, with the onset of severe occipital headaches, the patient started to go downhill. Nodules appeared on the right side of her face; the skin was infiltrated under the left costal margin and in the lower lumbar region, and the right side of the neck became œdematous. The abdomen was distended, with small veins round a protuberant umbilicus. The liver was felt one finger-breadth below the costal margin. Œdema of the left leg reappeared. Suddenly on Sept. 1 she became distressed and dyspnœic, with lapses of consciousness, and she died next day. She had been in hospital for 10 weeks.

POST-MORTEM FINDINGS

Necropsy.—Hæmorrhage from ulcerated secondary growth in stomach; generalised lymphosarcoma. *Cardiovascular*

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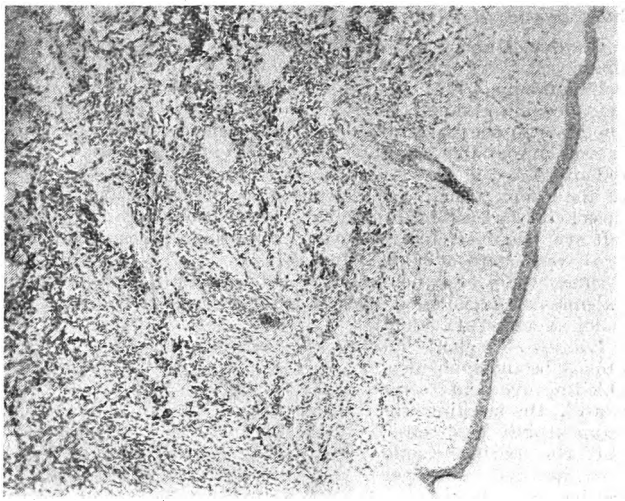

Fig. 2—Biopsy specimen from skin on margin of left orbit. (× 50.)

system: moderate atheroma; excess of free fluid in pericardium; anæmia of myocardium; ante-mortem clot in left common iliac vein and in branches of pulmonary artery in lower lobes of both lungs, with small subpleural areas of infarction at bases. *Respiratory system:* œdema of emphysematous lungs. *Alimentary system:* one submucous nodule in œsophagus at level of tracheal bifurcation; numerous nodules beneath mucosa of stomach and duodenum, one having ulcerated and showing an eroded vessel in its base; fluid blood in cæcum and in small intestine; one small submucous nodule in ileum. *Spleen and lymphadenoid system:* grey, in places pinkish-grey, and pink tissue taking the place of enlarged lymphatic glands in posterior triangles of neck behind pharynx and œsophagus, extending outwards to ensheathe brachial plexus on both sides; similar masses in posterior mediastinum and para-aortic regions, glands being poorly outlined and matted together by infiltration into surrounding fibrous tissue; similar tissue taking the place of moderately enlarged thymus; secondary mass in right 7th rib adjacent to costochondral junction; congested rather fleshy spleen about twice the normal size. *Central nervous system:* brain not examined; sarcomatous infiltration forming a mass outside dura in lumbar region of cord; rest of cord normal. Other organs showed no change beyond slight anæmia.

Histological Examination.—Lymphosarcoma consisting of small and medium-sized lymphocytes infiltrating fibro-fatty tissue of neck (fig. 3), fatty thymus, and brachial plexus (fig. 4). Lymphosarcoma also found in para-aortic lymph-gland and submucous nodule in stomach.

DISCUSSION

There is a type of recurrent facial cellulitis which this lesion resembled very closely at first. It was originally diagnosed as periorbital cellulitis secondary to ethmoiditis, though there was no obvious infection in the nose or sinuses. Later it resembled recurrent erysipelatoid attacks of the face as originally described by Sir Jonathan Hutchinson (1889). These lesions usually start as an œdematous swelling of the face. They may be localised, commonly to eyes, nose, or lips, or may involve the whole face. They may be heralded by signs of fever, with rigors, prostration, &c., though commonly there may be no constitutional disturbance. The swelling may change in size or shape, as did this one after the course of anodal galvanism, and may often disappear altogether, as this did after the biopsy specimen was taken. After several remissions it usually returns to produce a persistent localised "solid œdema" of the face with no pitting—and before the biopsy this was very much the clinical picture in the present case.

It is thought to be due to infection with a streptococcus of low virulence, and for this reason penicillin would be expected to cure it. However, Andrews (1946) and Sequeira et al. (1947) report cases resistant to systemic penicillin. Therefore lack of response to penicillin did not preclude this as a cause.

Another possible diagnosis was angioneurotic œdema; but against this was the absence of pruritus, and the lesion behaved unlike any allergic phenomenon and was totally resistant to benadryl.

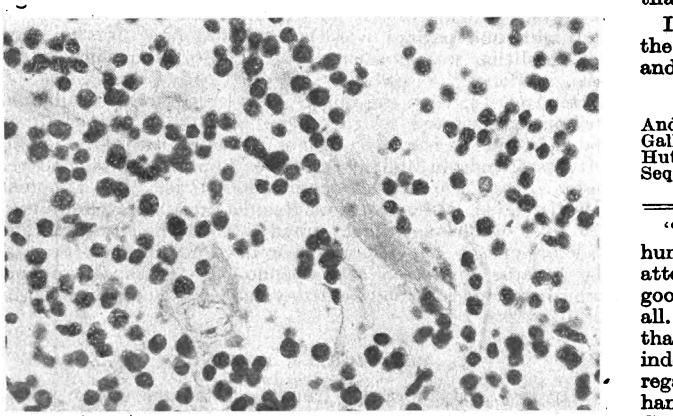

Fig. 3—Lymphocytes infiltrating fibro-fatty tissue of neck. (× 400.)

Fig. 4—Lymphosarcoma invading brachial plexus. (× 50.)

Mycosis fungoides *à tumeurs d'emblée* may closely resemble the present lesion as seen at the biopsy. This tumour presents first in the skin but may later develop in other organs or tissues and end fatally, sometimes quite rapidly.

Up to the time of the biopsy, the clinical picture in the present case was less like that of a sarcoma than that of a cutaneous inflammation.

I wish to thank Mr. W. A. Mill for his permission to publish the case, Dr. T. Day for his help with the pathological reports, and Dr. G. B. Dowling for his helpful suggestions.

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"... In the last twenty years I have seen and examined hundreds of children of all ages who have been in regular attendance at hospital since infancy and failed to find any good reason why they should have been taken to hospital at all. It is a dis-service to such children (and their parents) that they should be admitted to a special open air school or indeed have any special or unusual precautions taken in regard to their health. . . . No child should be regarded as handicapped whose only handicap is his mother."—Dr. R. P. GARROW, *Medical Officer*, Feb. 12, p. 71.

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Reviews of Books

Cardiology

WILLIAM EVANS, M.D., D.SC., F.R.C.P., physician to the cardiac department of the London Hospital. London: Butterworth. 1948. Pp. 310. 35s.

THIS is the companion volume to Dr. Evans's recent book on cardiography. All who know his work will welcome so convenient a reflection of his clinical teaching and writings. He does not set out to produce a standard textbook, discuss controversial problems, or provide references; nor does he deal with modern inquiries into such subjects as hæmodynamics, angiocardiography, or surgery of the heart; but he does give us a full and excellent guide to the practice of cardiology, emphasising diagnosis and treatment. The book is packed with practical wisdom and advice; among other things he recommends self-catechism during auscultation—a good habit which prevents many errors of omission. He has done much to differentiate added sounds and murmurs, and particularly those that may be wrongly attributed to organic disease and thus lead the doctor to restrict his patient's life unduly or engender neurosis. The stress laid on such signs as triple-rhythm may influence those who neglect or ignore these useful aids to diagnosis. Radiological findings (not dealt with in the volume on cardiography) are quoted throughout, and many reproductions of radiograms of the heart bear witness to their value. There is a chapter on diseases and disorders of the blood-vessels, and the book ends with advice on the general management of the cardiac patient. The text is bountifully and beautifully illustrated.

Some may regret the decision to limit precordial electrocardiograms to leads CR 1, 4, and 7, though undoubtedly this forms a satisfactory basis for routine work. Nor will everyone agree with Dr. Evans's definition of hypertension as "a systolic pressure of 180 mm. Hg or over and/or a diastolic pressure of 110 mm. or over in the presence of clinical radiological and cardiographic evidence of cardiovascular hypertrophy." Since not all Dr. Evans's views are—perhaps we should say, yet—generally accepted, a little caution should be exercised by those who still have to face examiners. But in practice there will be few difficulties.

Recent Advances in Respiratory Tuberculosis

(4th ed.) FREDERICK HEAF, M.D., F.R.C.P., senior medical officer, London County Council; N. LLOYD RUSBY, D.M., F.R.C.P., assistant physician, London Hospital. London: J. & A. Churchill. 1948. Pp. 290. 21s.

A NEW age demands a new outlook, and the authors of this fourth edition of the late Dr. L. S. T. Burrell's book start with the belief that recognition of the part played by social conditions and environment is the outstanding development in the study of tuberculosis in the past decade. Despite our knowledge of the tubercle bacillus, the epidemiology of this endemic disease has so far defied analysis. To its study the authors bring a catholic outlook, avoiding excessive emphasis on statistics on the one hand and uncontrolled generalisations on the other. The chapter on prognosis—always the most difficult to write—is a good example of their balanced view, being well founded on statistical records, yet giving due weight to experience of individual case-work.

On the epidemiological side, they discuss recent work on bovine tuberculosis and the milk problem, the fate of the tubercle bacillus outside the body (which is attaining new importance nowadays in the study of extradomiciliary infection), B.C.G., and vole-bacillus prophylaxis. But the most arresting facts in the epidemiological sections of the book are the statistical table showing the increase of meningeal tuberculosis since 1938, and the statement that in that year there were on the dispensary registers 71,997 persons in England and Wales who had at some time coughed up sputum containing tubercle bacilli, which, if not properly collected and destroyed, could infect other persons. The fine record of tuberculosis village settlements is rightly stressed: statistics demonstrate that, apart from their economic and curative value, such settlements contribute notably on the preventive side.

The fate of the initial infection, so much in the mind of the tuberculosis expert at present, is considered in an original manner under five episodes, in each of which the four variable factors—the number of bacilli, the degree of native and acquired resistance, and hypersensitivity—are regarded as playing a different part.

A full account is given of miniature mass radiography, and the new chemotherapy is adequately dealt with, in so far as so fluid a subject can be condensed into one short chapter. The sulphonamides, *p*-aminosalicylic acid, and the antibiotics, including streptomycin are all discussed. A chapter on complications faces some that are often slurred over in textbooks—notably enteritis and laryngitis, and bronchiectasis—and does not omit pregnancy. Collapse therapy, which has made rapid strides since the last edition was published, is also well described.

Reablement too has come into the foreground of the picture, and here the authors speak with special knowledge and authority in view of their connexion, as consultants, with the village settlements. The restoration to working conditions of a patient with a healed fracture is much easier than the reablement of a tuberculous person, who is always liable to break down again; and the account given of assessment of working capacity covers the ground as well as present experience and industrial conditions permit. Lastly, and perhaps most important, the book discusses respiratory tuberculosis in relation to the public-health services—a subject burked by most other textbooks.

Genetic-Statistical and Psychiatric Investigations of a West Swedish Population

TORSTEN SJØGREN. Copenhagen: Munksgaard. 1948. Pp. 102.

Professor Sjøgren has investigated the distribution of various mental disorders and the severer types of mental defect in a small island on the west coast of Sweden. The island has a population of about 9000 and represents a typical Swedish rural community. He aimed at identifying all cases of psychosis and oligophrenia in this population during the period 1900–44, and studying their familial distribution. The cases were discovered by a study of the parish registers, the records and the case-histories of the hospitals and asylums to which patients of the area could have been admitted, the records of the welfare institutions for the mentally diseased, and by extensive personal field studies. It is probable that the data are fairly complete for the frank severe psychoses and for the severer types of mental defect. Mild psychotics and psychopathics could be included only if they had been admitted to hospital, and are likely to be underestimated; nor could higher grades of mental defect be accurately estimated. The large body of material is presented critically and cautiously, and the method of identifying the various classes of case is described in full. The sex, year of birth, age at onset, mode of identification, and clinical diagnosis are given for each individual case, and the result is a valuable contribution to our knowledge of the population and familial distribution of mental diseases.

Virus Diseases of Man

(2nd ed.) C. E. VAN ROOYEN, M.D., D.SC. Edin., M.R.C.P.; A. J. RHODES, M.D. Edin. New York: Nelson & Sons. 1948. Pp. 1202.

THIS second edition, appearing after eight years, has the same general character as the first. With 270 more (and larger) pages it carries much new material and has been considerably rewritten. Revision of so large a mass of information is an immense feat, but there is much that might have been pruned away. Facts too freely reiterated may sometimes bury underlying principles.

The early chapters now offer a fuller account of electron microscopy, with some fine illustrations of the new "shadowed" technique, and a new section on the physicochemical properties of viruses. Diseases described for the first time include rubella (chiefly in relation to maternal rubella and congenital malformation), West Nile and other African viruses, Colorado tick fever,

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Newcastle disease of fowls, epidemic keratoconjunctivitis, Russian spring-summer encephalitis, Venezuelan encephalomyelitis, infective hepatitis, and homologous serum jaundice; but we cannot help regretting the absence of the rickettsioses. The sections on influenza, poliomyelitis, encephalitis, and pneumonia-producing viruses have been much enlarged.

Hæmagglutination has lately come to the fore and has wide implications in virus infections, but Professor van Rooyen and Dr. Rhodes only touch on this phenomenon in their accounts of the individual viruses that produce it, and ignore it in connexion with serological methods in general. Since no less than 9 viruses are now known to cause hæmagglutination, the phenomenon must have wide significance, with general implications for the mode of action of viruses on cells. Subsequent editions should allow the subject a worthier place in this solid work of reference.

Mikro-Methoden

zur Kennzeichnung organischer Stoffe und Stoffgemische. LUDWIG KOFLER, DR.PHIL. & MED.; ADELHEID KOFLER, DR. PHIL. & MED. Innsbruck: Wagner. 1948. Pp. 337.

THIS is a clearly written book on qualitative organic analysis by the mixed melting-point method. The authors describe an apparatus (which is now industrially produced at Innsbruck, Austria) consisting of a microscope fitted with a heater and either thermo-electric or exchangeable mercury thermometers. The latter are calibrated on the heater against known substances, and they avoid some of the inaccuracies which tend to occur when mercury thermometers are used for such purposes. Cooling blocks achieve rapid cooling of the apparatus after each estimation, and repeated estimations can thus be made at short intervals. Practical examples are included for those learning to work with this method, and extensive tables give the melting-points of organic substances in mixtures with two alternative test compounds. There is also a chapter on quantitative analysis of known organic substances in mixtures. The diagrams and photomicrographs are clear and well printed. References are mostly to Continental publications.

Psychiatry

A Short Treatise. WILLIAM A. O'CONNOR, L.M.S.S.A., D.P.M., medical superintendent, Ashwood House, Kingswinford, Staffs. Bristol: John Wright & Sons. 1948. Pp. 392. 35*s*.

IN his preface Dr. O'Connor stresses the cardinal importance of psychopathology, but his handling of this differs little from many another middle-of-the-road account, deferential to Freud but not Freudian, comprehensible but not profound. The clinical material is straightforwardly presented, rather more attention is given to historical developments in nosology than is usual, and treatment is described briefly and without much practical detail; mental deficiency is not dealt with, nor the applications of modern psychology, apart from psycho-analysis and its offshoots. Medical students would find the book sufficient for exam-passing purposes.

Medical Research in France During the War (1939-45)

Editor: JEAN HAMBURGER, professeur agrégé, Faculté de Médecine, Paris. Paris: Flammarion. 1948. Pp. 306.

THIS book appears three years after the war, through the help of the Rockefeller Foundation. It presents a series of thirty articles on widely differing subjects, both experimental and clinical, and is intended to show, as Professor Vallery-Radot writes in his short foreword, that French medical thought remained alive during the years of German occupation. Most of the work done was done under conditions of extreme difficulty, with shortages of equipment, animals for experiment, and even some such essentials as gas and electricity. Most of the authors of these reports were themselves under intense strain, and virtually cut off from all countries not under the control of Germany. R. Leriche writes on 800 lumbar gangliectomies, P. Giroud on vaccination against typhus, P. Blamoutier on digestive allergy, and R. Gutmann on early radiological diagnosis of cancer of the stomach; while papers on anti-histamine substances, hunger osteosis, aminothiazole in Graves's disease, and radiomanometry of the biliary tract offer remarkable testimony to the inventive minds and originality of French scientists, even during those desperate days. Some of the work has not been borne out by subsequent investigations, though part has fully justified the original findings. Not all the opinions given agree with English ideas; we should hesitate, for instance, to use a therapeutic test with intravenous protein for $1^1/_2$–2 months in the differential diagnosis of gastric cancer from ulcer. Nevertheless, English readers will welcome this opportunity of reading for themselves some of the work done in France of which they may have had little knowledge till now. It is a pity that the translation is at times a little clumsy.

A Surgeon's Guide to Local Anæsthesia

C. E. CORLETTE, M.D., F.R.A.C.S., consulting surgeon, Sydney Hospital. Bristol: John Wright & Sons. 1948. Pp. 368. 35*s*.

LOCAL anæsthesia is essentially a practical art and so can only be acquired properly by graduating from the dissecting and post-mortem rooms to the living patient. In the operating-theatre the guiding hand and personal touch of an experienced teacher turns the novice into a skilful local anæsthetist. Books, nevertheless, are essential, for few are so fortunately placed that they can learn local anæsthesia without them; and such books must be judged by the extent to which they give the apprentice a substitute for a master. By this standard Mr. Corlette largely succeeds, for his text talks, and in so doing gives colour to the descriptions, practical details, and wise hints.

His style is lively, but the printed word alone can never effectively call up the mental pictures which are needed for the art of local anæsthesia, and illustrations are therefore of the first importance. Here the book does not quite come up to the high standard of the text. Too many of the illustrations are sketchy, and in future editions should be better drawn, clearer, and more helpful.

Mr. Corlette's inspiration comes largely from the early continental writers, of whom Braun is the chief and to whom he pays repeated tribute. Perhaps this may account for the inclusion of a few rather obsolete techniques such as the orbital, and suprazygomatic approaches to the maxillary nerve, and the suprahyoid injection of the back of the tongue. Even so the book might truly realise the trade puff of "classic," were it not for Mr. Corlette's vigorous objection to local anæsthesia being administered by any other than the surgeon. He derides the professional anæsthetist (who after all is only relieving the surgeon of a tiresome preliminary) with some of the tartness of an old-fashioned pamphleteer. But he weakens his case by saying later that "the technique can be taught to young graduates in their periods as resident medical officers in hospital."

Books written with spirit and enthusiasm are all too rare, and we hope that this one, revised and better illustrated, will see many editions.

Diseases of the Skin (7th ed. London: Henry Kimpton. 1948. Pp. 1462. 90*s*.).—Prof. Oliver S. Ormsby and Prof. Hamilton Montgomery have thoroughly revised the seventh edition of this American work, which is probably the most comprehensive textbook on dermatology in the English language. New illustrations and colour-plates of a fine quality have been added, and the full bibliographies in each section, one of the most useful features of the book, have been carefully brought up to date. It is a work for teachers and specialists, and for reference, rather than for students and practitioners, but it should be in all medical school libraries.

Gynæcological and Obstetrical Anatomy. (2nd ed. London: Edward Arnold. 1948. Pp. 241. 40*s*.).—It has been said that good surgery depends on a smattering of anatomy, a profound knowledge of pathology, and an infinite fund of common sense. This book, by Prof. C. F. V. Smout, in collaboration with Dr. F. Jacoby, provides the gynæcologist with more than an ordinary ration of the first, and it never forgets his practical needs. Great industry has gone to its compilation in concise form, and in the new edition its scope has been widened in the more speculative realms of pelvic physiology—e.g., in the chapter on ovarian endocrine function and its control. Many of the illustrations are a joy to behold, and to postgraduates, studying for higher examinations in diseases of women it will come as a lively stimulus.

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THE LANCET

LONDON: SATURDAY, FEB. 19, 1949

English Mental Care through American Eyes

RECENT books by former patients have given a discouraging account of life in public mental hospitals,[1] and we publish this week the rather unhappy experiences of a doctor who entered a private hospital as a voluntary patient. But if there is much room for improvement here, it seems that conditions are, to say the least, no better in many of the State hospitals in America. An article in *Life*, early in 1946, carried photographs of patients in such hospitals who appeared much neglected; and the story told by a former attendant in two State mental hospitals [2] is a painful description of the humiliations and hardship which patients often suffer, and the inhumanity engendered in those employed to care for them. Dr. DALLAS PRATT, who in 1947, on behalf of the American National Mental Health Foundation, made a survey [3] of 16 English public mental hospitals, thought our standards, on the whole, much better than those in the United States—despite the high level of care in such famous American hospitals as the Phipps Clinic and the Institute of Living.

Since Dr. PRATT's aim was to indicate practices that backward State hospitals might usefully follow, he dwells more freely on our highlights than our black spots; but it is encouraging to learn there are enough of these to strike a stranger's eye. His experience was not confined to our best hospitals (though these formed a large proportion of the 16); he deliberately visited 4 of "less progressive type," of which 2 were definitely backward. From information given him, he graded the 101 mental hospitals in England and Wales as: "progressive," less than a quarter; "average," more than half; "backward," a quarter. Judged by the same standard, he thinks that half to three-quarters of American State hospitals could be classed as backward, and that most of the rest are average; "very few indeed can be considered progressive." It would be interesting to know the information on which this grading was made. We cannot call to mind any official report giving the necessary data, and it seems likely that it was founded on impressions of members of the Board of Control, or on material available to them. If so, our own medical profession would welcome the opportunity to share the information given to Dr. PRATT.

He was particularly impressed by the fine grounds, freely used by patients, which surround many of our mental hospitals; by the curtains, flowers, and unbarred windows which give a pleasant atmosphere to wards and day-rooms, regardless of whether they house quiet or disturbed patients; by the absence of physical restraint (he saw leather cuffs, such as are used in America today, exhibited with chains and manacles as relics of an archaic age); by the general use of occupational therapy; and by the fact that our mentally sick are looked after by nurses, trained or in training, and not by attendants. On the last point he may not have fully realised the difference between State registration and the certificate of the Royal Medico-Psychological Association. Since the certificate was withdrawn, the mental section of the State register has offered the only qualification open to mental nurses; and it may be that fewer mental nurses will take this than were wont to take the R.M.P.A. examination. In the coming years this may result in a fall in the number of "trained" mental nurses, and a rise in the proportion of assistant and part-time nurses—without any change whatever in the type of men and women undertaking the work.

Dr. PRATT also approved the continuous supervision of our mental hospitals by the Board of Control, their small size compared with American hospitals, the low two-story buildings, the self-contained admission units, the high proportion (54·2% of admissions in 1946) of voluntary patients, the adequacy of linen and bedding, the individual look of patients' clothing, the widespread use of physical therapies, and the many outpatient clinics attached to mental hospitals. No less than 15 of the 16 were running their own outpatient clinics, staffed by the hospital psychiatrists. Some of these clinics were held in the mental hospitals themselves, but more were held in the general hospital of the area. Some hospitals were running several clinics—thus Mapperley has nine, Warlingham Park three, and Netherne reported 4000 outpatient sessions during the year. In 1943, when Dr. C. P. BLACKER made his neurosis survey, there were 216 psychiatric clinics in England and Wales, all but 66 of them being based on mental hospitals. This gave 1 clinic to every 170,000 people, which Dr. PRATT compares with 688 clinics in the United States, in 1946, or 1 clinic to every 204,000 people. Such clinics, he notes, benefit the mental hospitals themselves, since they bring the staff face to face with the community's need for a better mental-health service, and stimulate them to provide it.

Against these compliments must be set some adverse findings. One of the 16 superintendents was "opposed in principle" to occupational therapy, saying that enough occupation was provided in his hospital by the "clipping of hedges, the carting away of rubbish, and the digging of holes." This habit of regarding the patient as a form of cheap labour for the use of the hospital is most undesirable. In the better hospitals it is recognised that if occupation is to be used as a remedy it must serve the needs of the patient, in preference to the needs of the hospital administrator. Dr. PRATT also found that some county councils are inefficient and unduly hampered by red tape, and that some poor areas have maintenance-rates which are too low—though even the lowest, he says, are more than double the lowest rates in the U.S.A., and the average is about half as much again as the American average. He was writing before the National Health Service was launched; under it, these economic differences can surely be adjusted. It might even be possible, on

1. *Lancet*, 1947, ii, 880.
2. Orlansky, H. *Politics*, 1948, no. 3, p. 162.
3. Published by the Foundation, 1520, Race Street, Philadelphia 2, U.S.A. 1948. Pp. 28. $.50.

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some grant-giving plan, to encourage backward hospitals to bring their standards up to those of the best. This is the system applied to general hospitals by King Edward's Hospital Fund for London, and it has been singularly effective, over a period of years, in persuading the laggards to modernise their kitchens, improve their nurses' quarters, increase the staffing of their almoner's departments, or take other welcome steps towards perfection. Mental hospitals work so much in isolation, each a little cosmos under a senior officer whose word is law, that they have few chances of emulating one another. A grant-giving body such as the King's Fund could help them to develop a spirit of healthy rivalry.

Dr. PRATT was also disappointed with some of our mental hospital equipment, notably the X-ray plant, laboratories, and lavatory accommodation. The last he found to be inadequate in some mental hospitals—surely a serious indictment at a time when the wards are notoriously overcrowded. He also finds us more prone to give physical than psychiatric treatment to the mentally ill, and was a little dubious of the use made of sedation in one of the hospitals he visited. (It will be remembered that the patients who have written books on life inside our mental hospitals agree in thinking that sedation is often used for the convenience of the nurses rather than the benefit of the patients.) Finally, Dr. PRATT observed that the psychiatrists, nurses, occupational therapists, and social workers attached to our mental hospitals are too few, as we well know. Thus the picture is in some respects imperfect even to the eye of the kindly visitor. But the number of mental hospitals in the whole country is so small that it should not be beyond us to make them an absolute credit to the great pioneers of humane treatment for the mentally sick.

The Oximeter

THE theoretical basis of cyanosis is now well understood. Oxyhæmoglobin is bright red, while reduced hæmoglobin is darker and bluer. It is the undue preponderance of reduced hæmoglobin in the skin capillaries that makes some people look purple or blue. The blueness may result from imperfect oxygenation of the blood leaving the left heart. This, in turn, is consequent on defective oxygenation in the lungs or even partial bypassing of the lungs, as in congenital heart disease, and is called cyanosis of *central* origin. In *peripheral* cyanosis, on the other hand, the blueness results entirely from a local disturbance of the circulation, with sluggish blood-flow and excessive removal of oxygen by the tissues from the relatively stagnant blood. Hitherto the clinical differentiation of the two types has been based simply on appreciation of their existence combined with shrewd guess-work. Examination of a sample of arterial blood will often decide, but many clinicians hesitate to adopt this procedure, and in any case the prompt analysis of samples for their gas content requires laboratory facilities which are not found in every hospital.

The possibility of using optical methods for estimating the degree of oxygen saturation of arterial blood has been recognised for at least fifteen years.[1] Oxyhæmoglobin transmits red light more readily than reduced hæmoglobin does, and by using a photo-electric cell with appropriate filters the percentage of the total hæmoglobin which is formed by oxy-hæmoglobin can easily be calculated when these pigments are in solution. The same method is applicable, though with less accuracy, to whole blood, and SQUIRE [2] applied the device to transilluminated living tissues. This device was further developed by GOLDIE [3] and MILLIKAN [4] during the late war, when it found a special place in the study of the reactions of airmen exposed to low oxygen pressures. The impetus of these technical advances is now being felt in ordinary clinical investigation. The oximeter, as the apparatus is called, is being increasingly used in the United States. It consists of an ear unit fitting over the pinna, with an electric bulb in front and a photo-electric cell behind. The heat generated by the bulb dilates the vessels of the ear and increases the blood-flow sufficiently to make the ear blood equal in oxygen content to the arterial blood. Galvanometers connected to the instrument indicate the amount of light transmitted by the ear, and hence the oxygen saturation of arterial blood can be estimated. The method, however, is not yet completely accurate when used in this way, as Beer's law relating to optical density of translucent solutions cannot apply exactly to whole blood in tissues. Thick ears and thin ears add to the variables. The method has an error of 3–7% in absolute readings. But it reveals changes in a patient's oxygen saturation much more exactly. In a normal person the arterial blood is 95% saturated with oxygen. If he is given oxygen to breathe the oximeter reading will rise about 5% as the hæmoglobin becomes fully saturated. This forms the basis of an informative test.

By observing these oximeter responses GODFREY and his colleagues [5] have obtained some useful clinical data. A rise of more than 5% in the arterial oxygen saturation indicates previous subnormal saturation. In patients with congestive heart-failure the oximeter response to oxygen breathing was usually about 10–15%, showing a definite but moderate degree of arterial unsaturation (85–90% saturated). The response of patients with primary pulmonary disease was mixed. Sometimes there was a remarkable improvement in arterial oxygen saturation on breathing oxygen—in one case + 27%—but sometimes the response was relatively small, possibly because the blood was continuing to flow through completely unaerated parts of the lungs, so that even oxygen inhalation could not correct the deficiency. Similarly poor responses would be expected in the blue forms of congenital heart disease, where blood is shunted from the right to the left side without going through the lungs at all. A further report by GROOM et al.[6] shows how the oximeter can be adapted for use with cardiac catheter studies in obscure congenital heart disorders. The exploration of such hearts by this technique is no easy matter, and an immediate approximation to the oxygen saturation of blood drawn from various positions within the heart is of immense value to the investigator. The Mayo Clinic investigators simply draw blood back through a transilluminated polythene tube, the light falling on an oximeter cell. This permits immediate recognition

1. Kramer, K. *Z. Biol.* 1934, **95**, 126.
2. Squire, J. R. *Clin. Sci.* 1940, **4**, 331.
3. Goldie, E. A. *J. sci. Instrum.* 1942, **19**, 23.
4. Millikan, G. A. *Rev. sci. Instrum.* 1942, **13**, 434.
5. Godfrey, L., Pond, H. S., Wood, F. C. *Amer. J. med. Sci.* 1948, **216**, 605.
6. Groom, D., Wood, E. H., Burchell, H. B., Parker, R. L. *Proc. Mayo Clin.* 1948, **23**, 601.

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of the approximate composition of the blood in different parts of the abnormal heart, greatly facilitating the accurate analysis of some of these puzzling defects which, in carefully selected cases, are now yielding to surgical treatment.

How to Change Food Habits

THE "food advice" activities fostered by the Ministry of Food since early in the war are now to be transferred to the Ministry of Education. One may hope that some person or some committee will take the opportunity to review the work of the last few years and consider what we are really attempting in this important task of instructing the public in the elements of sound nutrition. If is, of course, a branch of what is usually called health education. But in the public mind feeding is something far more than a matter of health; and the teaching has obviously to be of a subtle and pervasive nature. Moreover, as LE GROS CLARK [1] has pointed out, we had better cease to think of such advice as merely an expedient for guiding the country through its period of austerity, and decide rather on a more permanent scheme of formal and informal instruction.

Many efforts have been made to instruct the "labouring classes" in the principles of feeding since the "Food Exhibition" opened at South Kensington in 1856. A year or two later EDWIN LANKESTER wrote the guide to the exhibition, giving a clear scientific exposition of the chemistry of food, as it was then understood, and of the functions of food in the human body. Yet few have paused to meditate upon this peculiarly elusive form of popular enlightenment. No doubt psychologists could give us some guidance; for food is one of those matters most subject to unconscious and half-conscious prejudices. A man may readily admit that authority has some right to suggest to him that his child shall be immunised against diphtheria, but he inclines to be more resistant when it is a question of his traditional habits and tastes at the meal table. Nevertheless a community, if it would in fact benefit from a modified or more flexible dietary, can in the long run be persuaded to adopt it. The change may take years or even generations; and those who promote it should have a due sense of proportion and humour. Yet it can be done, especially if we begin with the young child; and the transfer of food instruction to the Ministry of Education makes this more feasible. The Ministry of Food, and before the war the local health authorities, were concerned mostly with the informal instruction of the adult, but we can now picture a process of teaching that will unobtrusively accompany the individual through all the stages of life. Indeed it would not be difficult to produce a "model" scheme, capable of being merged into the normal course of education and calculated to touch people where they are likely to be most receptive. The trouble with those who advance such schemes is that they commonly assume that the whole plan must be put into operation immediately, whereas we should rather be aiming at its gradual realisation. These things take time; and here time happens to be on our side. Men will continue to eat while the world lasts, and the only question we have to ask ourselves is whether it is desirable, in so important a matter as nutrition, to set going a continual leaven of instruction upon the elements of a normal diet. Is it, in brief, our business progressively to get people both to understand what a sound diet is and to acquire a taste for it?

The teaching of nutrition is not so serious, nor on the other hand so easy, as some writers seem to suggest. It cannot be so very serious; for, after all, in our own country the general health, and so presumably the average diet, is obviously fair to good. It is not easy; for the method of presentation, the timing, and the form of instruction all need to be carefully studied. For instance, though the Ministry of Food undoubtedly reached a large body of housewives, some 10–20% of them have proved much less receptive and much less easy of access. Through what medium can these women be reached? The evolving food habits of each new household are the product of two patterns of taste and tradition; and, though a considerable proportion of young women today come to their domestic duties with some knowledge of cooking and of food values, acquired at school, one wonders how many of the young men have absorbed even the rudiments of food instruction. Of course, the country cannot immediately create the machinery for reaching the 10–20% of women who seem to elude our influence, or even for providing schoolboys with simple lessons in food preparation and food values. But that is not the problem. The problem we first have to put to ourselves is precisely how a civilised community would devise a scheme of nutrition education which could in time gradually develop into a broad current of useful instruction. The recent experience of the Ministry of Food has probably been of value, but that experience should be carefully analysed. Whatever the effect of the work done, none of us will deny the vision of a Ministry that set itself, through the activities of a small body of able women, to make the people conscious of its basic food requirements. In changed circumstances the same vision can help us to consolidate the gains we have made through the last ten years, in our common stamina and power of survival.

The Value of Curiosity

IN his Hunterian oration before the Royal College of Surgeons last Monday Mr. H. S. SOUTTAR spoke of the resentment which our forefathers felt at any interference with what were regarded as established facts. "It was through this veil of prejudice and ignorance that John Hunter and his museum tore so completely, and it is this achievement which so amply earns our gratitude. The specimens in his collection are themselves of value, but of greater moment is the lesson they teach us of the value of observation." Some men are incurious, others curious. "We all recognise the man to whom discovery is the breath of life and the man to whom it is anathema. The latter is often a first-class teacher who not unnaturally fears the disturbance of his mental categories: the former may be a great researcher but is often entirely unintelligible to his pupils." The one essential factor in observation, Mr. SOUTTAR believes, is curiosity; and there are many kinds of curiosity from a mere desire to interfere to an urge to satisfy some deep longing for comprehension. "Whatever its nature it is undoubtedly an instinct essential for fruitful observations, and one with which every teacher should seek to inspire his pupils. In John Hunter it was almost a mania and it was the steady driving force behind all his work."

1. Clark, F. Le G. *Lancet*, 1947, i, 721.

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Annotations

A QUESTION OF COST

ANYONE who has bought a business—or for that matter a medical practice—knows that the vendor's balance sheets are a poor guide to his own immediate prospects. Only after he has taken over can he tell the size of his clientele, the precise extent of the liabilities he has incurred, and the cost of necessary repairs; and at first he may have to make repeated incursions into reserves.

Something of this sort seems to have befallen the Government in taking over the medical services. A year ago the gross cost of these services for the whole of Great Britain for the nine months ending on March 31, 1949, was estimated at £198,376,000; after deduction of appropriations in aid totalling £48,701,000 (of which £27 million was to be derived from the National Insurance Fund) the net cost to the taxpayer was set at £149,675,000.[1] In the event this sum has covered barely three-quarters of the cost now anticipated; and Parliament has been asked for a further £58,455,000.[2] This means that the taxpayers' contribution to the service in its first nine months is at the rate of just under £4 10*s*. per head of population. The two estimates apportion the gross cost for England and Wales as follows (the proportions for Scotland are much the same):

Service	*Original estimate* £	*Revised estimate* £
Advances to regional hospital boards	95,518,000	109,584,000
Advances to boards of governors of teaching hospitals	10,349,500	18,629,500
Payments to the Ministry of Pensions	130,000	500,000
Grants to local authorities	3,750,000	9,283,000
Administration	890,000	1,606,000
General medical services	27,500,000	29,800,000
Pharmaceutical services	11,450,000	16,225,000
General dental services	7,150,000	19,000,000
Supplementary ophthalmic services	2,080,000	13,500,000
Liabilities transferred to the Minister	2,196,000	18,605,000

A small part of the discrepancy is no doubt accounted for by the unexpected popularity of the new service; a year ago few foresaw that within the first six months some 95% of the population would choose to benefit. On the other hand, many predicted immediate demands by those who, though needing dental or ophthalmic treatment, had hitherto foregone it; and with this leeway to make up the first estimates for these two services were frankly unrealistic. Where, as in this case, an official estimate has been greatly exceeded, there is naturally suspicion of extravagance; and it is therefore well to bear in mind that no less than £39,679,000 of the £75,719,000 gross increase in the new estimates quoted above is absorbed by these two services, the cost of which is likely to tail off somewhat, and by liabilities transferred to the Minister—a non-recurring expense unconnected with the actual operation of the service. If the revised estimates prove anything, it is not the extravagance of the new organisation but the deficiencies of the old. The medical services are the concern of all; and it would be damaging to all if expenditure were deliberately curtailed before ancient deficiencies are made good. Later years will show whether the work of repair is satisfactory.

1. Civil Estimates for the Year ending March 31, 1949. Class 5: Health, Housing, Town Planning, Labour, and National Insurance. H.M. Stationery Office. 1948. See *Lancet*, 1948, i, 532.
2. Supplementary Estimate, 1948–49: Civil Estimates and Estimates for Revenue Departments. H.M. Stationery Office. Pp. 117. 2*s*.

TRICHLORETHYLENE AS AN ANALGESIC IN LABOUR

A COMMITTEE of the Royal College of Obstetricians and Gynæcologists have completed an investigation,[1] financed by the Birthday Trust Fund, into the use of trichlorethylene, given by the improved model of the Freedman bottle, as an analgesic in labour. As a result of their findings the council of the college have decided that they cannot recommend the method for use without supervision by midwives engaged in domiciliary practice—a decision which has caused widespread disappointment and which Dr. Freedman criticises in our correspondence columns this week.

Sixteen hospitals took part in the study, and each appointed a supervisor, or observer, to be in charge of the investigation and report on the cases. The method was studied in 2354 cases. Between 70 and 80% of the mothers were pleased with it, some were doubtful, and only a few (under 7%) were dissatisfied. The observers found that analgesia can be achieved without any high degree of skill on the part of the administrator, and that the method relieves pain equally well when combined with other analgesics in difficult labours. If the mother is very nervous the method becomes less effective, but even in this group over 60% were pleased, and only 12–14·4% dissatisfied. In the opinion of all the observers a high proportion of cases obtained adequate relief, and in the series as a whole the method produced better analgesia than Minnitt's gas-and-air machine. They found that a small proportion—under 5% of patients—became uncooperative, mainly because they were too sleepy to push in the second stage; a few were restless. The incidence of drowsiness or restlessness does not seem, they say, to have any relation to the duration of administration; nor does the method appear to affect either the forceps-rate or the obstetric-interference rate. There is no evidence that the method has any influence on the maternal-mortality rate. The tachypnœa associated with an overdose of trichlorethylene never appeared in this series. In 6 cases out of the 2354, trichlorethylene was suspected of causing bradycardia or arrhythmia of the maternal heart; 3 of these cases had pethidine as well. It was not certain that trichlorethylene was the cause of these pulse irregularities, and the observers did not think them of much significance. A few women refused trichlorethylene because of its smell, and some observers thought it caused vomiting occasionally.

Opinions were divided about the effect on the fœtal pulse-rate, some observers finding no reason whatever to suspect the method as a cause of fœtal distress. In the 18 cases where trichlorethylene was held by an observer to be a cause, or contributory cause, of fœtal distress, the fœtal pulse-rate slowed to 100 or below. Of these 18 cases 11 were in one hospital, and the observer in this hospital therefore believed that trichlorethylene can only be used safely as an analgesic if this possibility is appreciated, and the fœtal heart-rate watched. On the other hand, there is no evidence that trichlorethylene influenced the stillbirth-rate or the neonatal death-rate in any way in this series. Nor does the incidence of asphyxia neonatorum seem to be affected where trichlorethylene is given alone.

These favourable findings led the majority of the observers to decide that they would happily be responsible for a district in which trichlorethylene was given by domiciliary midwives trained in this method. Two observers thought that unsupervised midwives might give the drug for longer periods than was customary in this series, and two were against its use by midwives

1. Nineteenth Annual Report of the Royal College of Obstetricians and Gynæcologists for the Year 1947. Obtainable from the Royal College, 58, Queen Anne Street, London, W.1.

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because of the occasional effects on the fœtal pulse-rate (0·8% of cases) and the occasional non-coöperation of the mother (4·6% of cases). Prof. R. R. Macintosh reported to the committee that the concentration of trichlorethylene vapour delivered by the Freedman bottle is not constant, but varies, at temperatures ranging from 17 to 35°C, from 0·42 to 1·15%. It also varies with the rate of flow.

Dr. P. J. Helliwell and Dr. A. M. Hutton, research fellows of the Association of Anæsthetists, themselves acted as observers, collated the material and wrote the report; and in a postscript they offer their own opinions on the method. They conclude that it is unsuitable for the unsupervised midwife because the concentration of vapour varies not only with temperature but also with the amount of shaking the bottle gets, and the depth of the mother's respirations. The mother's tolerance also varies, and the fact that uncoöperative stupor has been seen occasionally under the conditions of the test suggests, they think, that a state of anæsthesia might sometimes be induced if trichlorethylene were used under less ideal conditions. They fear, too, that it might be "misused," presumably by administration in excess; though, on previous form, we should have thought midwives more likely to give too little than too much. Meanwhile the council of the college promise that further attempts will be made to produce an apparatus that will fulfil all requirements.

TEN USEFUL YEARS

When the Nuffield Provincial Hospitals Trust was set up in 1939 the coördination of hospital and medical services had been under consideration of varying intensity for at least twenty years. But in the 1940s the pace of social reconstruction quickened, and with the passing of the National Health Service Act in 1946 the emphasis of the trust's work has shifted. The record of its first ten years [1] shows how much it contributed, by lucid fact-finding and intelligent experiment, to the new service. The trust's original plan, set out in an appendix to the report, was dropped after the announcement of the Government's post-war hospital policy in 1941. But the hospital regions which the trust proposed are roughly the same as those that have been adopted, and many of the joint advisory regional and divisional councils which the trust established have made easier the task of the statutory bodies which have followed them by their informative reports on local problems and on the organisation of regional services for the different specialties. Another important side of the trust's work—the surveys of hospital services in different areas—was continued in coöperation with the Ministry of Health. The seven provincial surveys were conducted by the trust and three others by the Ministry with common terms of reference. The conclusions of all ten were summarised by the trust in the Domesday Book of the Hospital Services. The trust has compared these surveys to the stretching of a tapestry upon a frame: "it showed up equally the good strong fabric, the weak, threadbare, and cobbled patches, and the holes," and it has been quick to help to make good the defects it discovered. In giving such aid its policy has been to foster coördination between municipal and voluntary hospitals, local authorities, and universities, and to give opportunity for practical demonstration of accepted theory. Perhaps the most notable of these stimulating projects has been the establishment of chairs in social medicine at Oxford and at Birmingham, in child health at Durham and at Belfast, and in psychiatry at Leeds. The trust has also made generous grants to set up health and sickness record bureaux at Oxford and Glasgow, to the industrial health service at Slough, and to assist the recruitment and training of nurses.

In discussing its plans for the future the trust disclaims equally the view that its work has been (*a*) completed and (*b*) frustrated by the National Health Service. Responsibility for coördination of the hospital services now rests with the Government, but, as the trust rightly points out, there is much still to do in linking more closely hospitals and the ancillary medical services including those, such as industrial health, which do not come under the Act. The experimental mobile meal service which it has sponsored at Thurrock, for instance, is an example of coördination between hospital, general practitioner, and local-authority service. Again though the principle of coördination has been accepted by the Act many practical difficulties await solution. As a fact-finding body, the trust's objectivity and freedom of approach have special value and it has lately undertaken two investigations of outstanding problems: a job-analysis of a nurse's work and an inquiry into the functions and design of hospitals. The trust sums up its plans for the future as study, experiment, and demonstration, and it looks as though its next ten years are to be busy and useful.

1. Nuffield Provincial Hospitals Trust 1939–48, 12, Mecklenburgh Square, London, W.C.1. Oxford: University Press. 1949. Pp. 54.

PROPHYLAXIS OF OPHTHALMIA NEONATORUM

In Scotland it is obligatory on midwives to instil silver nitrate into the eyes of newborn babies as a preventive of ophthalmia neonatorum. In England and Wales, too, silver nitrate instillation is widely used and harks back to the days of Credé. There is no doubt that the Credé method has greatly reduced the frequency of ophthalmia neonatorum; but, as Sorsby [1] pointed out, this procedure consists of two distinct components—asepsis and antisepsis. The toilet of the babies' eyes is sound asepsis; the instillation of silver nitrate or other antiseptic reflects Listerian influences prevalent in Credé's day. In silver nitrate Credé was choosing an agent which was then credited with more properties than would seem reasonable today. The large number of substitutes for silver nitrate that have been advocated since Credé died in 1892 suggests that silver did not give all the satisfaction with which it is usually credited. Of late years it has indeed been questioned whether silver nitrate has any value at all in the prophylaxis of ophthalmia neonatorum. In a study of the incidence of ophthalmia neonatorum in over 220,000 births at 45 obstetric centres during 1938–42, Sorsby found that in 92,865 births where preparations other than silver nitrate were used the frequency of gonococcal ophthalmia neonatorum was 0·7 per thousand births, whereas at centres where silver nitrate was used the rate was 1·0 per thousand. There are no reliable statistics on the frequency of ophthalmia neonatorum in births where no prophylactic drops were used at all, and in any case such statistics have to be interpreted against the general level of obstetric efficiency prevalent at different centres. It is clear, however, that silver nitrate does not always suppress the development of gonococcal ophthalmia neonatorum, and there seems to be no reason to believe that it is more efficacious than other agents, some of which are of very doubtful value.

Taylor and Calman [2] found organisms—mainly staphylococci and coliform bacilli—in the conjunctival sac of only 6 out of 340 babies immediately after birth, and none of these subsequently developed eye infections. They repeated their bacteriological test 7–10 days later in 220 infants, of whom 102 had received a drop of silver

1. Sorsby, A. Ophthalmia Neonatorum. London, 1945.
2. Taylor, M. D., Calman, R. M. *J. Obstet. Gynæc.* 1948, 55, 641.

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nitrate as a prophylactic measure and 118 were untreated; in both groups there was now a considerable incidence of organisms in the conjunctival sac: 17·6% in the treated group and 15·4% in the untreated. Clinically many of these eyes were not infected, though the organisms recovered were of the same variety as recorded by Sorsby for cases of ophthalmia neonatorum, except that there was no instance of the presence of gonococci. This study suggests that a drop of 1% silver nitrate does no harm, but there is surprisingly little evidence that it does any good.

The instillation of a drop of antiseptic into an eye with the object of disinfecting it is essentially illogical. Drops are washed out from the eye within a few minutes, and neither a classical antiseptic or one of the new antibiotics can be expected to achieve disinfection by a single application of momentary efficacy. The prevention of ophthalmia neonatorum is hardly a question of disinfecting an infected conjunctival sac. The aseptic component of the Credé procedure—toilet of the baby's eyes—is reasonable and should be practised in all cases. Even this would become superfluous if we could ensure a sterile vaginal tract in all mothers. The realisation that the gonococcus plays quite a subsidiary rôle in ophthalmia neonatorum as seen today, and that almost any type of maternal infection can produce ophthalmia neonatorum, crystallises the issue of prophylaxis as a purely obstetrical problem. But it is by no means an insignificant issue, for some 4000 cases are still being notified every year.

CALCIFEROL AND STREPTOMYCIN IN LUPUS

THE treatment of cutaneous tuberculosis with calciferol, evolved independently by Charpy in Dijon and by Dowling and Prosser Thomas in London, seemed to involve a danger of "metastatic" calcification; the risk was that calcium mobilised by the action of the vitamin might be deposited in tissues such as the renal tubules, the arterioles, the media of large blood-vessels, and possibly the retina. Many were surprised to find that, though other anticipated complications occurred, there was only a single report of metastatic calcification. Lately, however, Howard and Meyer[1] have reported that of 10 cases of vitamin-D intoxication 1 showed evidence of gross vicarious calcification in subcutaneous or renal tissues, while in 9 cases the characteristic eye lesions were detected on slit-lamp examination.[2] (In these American cases large amounts of vitamin D were given. The highest daily dose was 600,000 units, the lowest 150,000 units; and the period of treatment with calciferol ranged from 2 to 18 months.) The patient in whom metastatic calcification was observed was a man of 59 with rheumatoid arthritis who received 500,000 units daily. A thin line of yellow deposits appeared along the outer borders of his lips; his finger-nails became tender, with yellowish-white deposits underneath them; and on his trunk, limbs, and face an eruption resembling prurigo nodularis appeared. Biopsy of these lesions revealed senile elastosis with patchy deposits "apparently of calcium" in the mid-corium. His serum-calcium was 14·3 mg. and serum-phosphorus 4·6 mg. per 100 ml. The lesions under his finger-nails were opaque to X rays, but those in his lips were translucent. Slit-lamp examination of the eyes showed conjunctival crystalline deposits and band keratitis lesions. After 19 months the skin eruption remained, though the serum-calcium was within normal limits; the conjunctivæ were almost free of crystals.

In lupus vulgaris the risk of toxicity may, it seems, be largely overcome by combining calciferol with streptomycin treatment. Cornbleet[3] has described 5 cases where calciferol was given for 5–12 months, by which time it ceased to be of benefit. Streptomycin was then given in conjunction with calciferol until the lesions appeared to be inactive; this took 6–9 weeks. In all cases 1 g. of streptomycin was given daily in divided doses at 4-hourly intervals. The dose of calciferol was 100,000 international units daily; and symptoms suggesting intolerance developed in only one patient, a negro who complained of giddiness and nausea and vomited a few times in the first week. In an addendum Cornbleet refers to 2 patients who were given calciferol and streptomycin ab initio; both were free of visible lesions in 7–8 weeks.

The effect of the combined treatment was so rapid and impressive that Cornbleet postulates a synergistic action between the antibiotic and the vitamin. Some time will pass before it is known whether these cases are cured; but this early report suggests that a combined attack may prove highly satisfactory; and some other maladies, such as sarcoidosis, may also respond to it.

1. Howard, J. E., Meyer, R. J. *J. clin. Endocrinol.* 1948, **8**, 895.
2. Walsh, F. B., Howard, J. E. *Ibid*, 1947, **7**, 644.
3. Cornbleet, T. *J. Amer. med. Ass.* 1948, **138**, 1150.

F. H. A. MARSHALL

Francis Hugh Adam Marshall, F.R.S., who has died at the age of 70, will long be remembered for his studies on the physiology of reproduction. Almost the whole of his academic life was spent in Cambridge, but it was during a spell in Edinburgh that his interest in this field was first aroused. He had gone there to work with Cossar Ewart on telegony. This research proved comparatively fruitless; but, stimulated by the writings of Walter Heape and by the resources of Cossar Ewart's department, Marshall turned his attention to the œstrous cycle, first in the sheep and then in the ferret and dog. His paper on the cycle in the dog, published in the *Transactions of the Royal Society* in 1905, was accompanied by a communication on the ovary as an organ of internal secretion, in which he set out the hypothesis that the œstrous cycle was regulated by the alternating action of hormones produced by the graafian follicle and the corpus luteum. Twenty-five years elapsed before this far-sighted idea was fully vindicated, but in the meantime Marshall's influence did much to give balance to the subject. His later researches proceeded in more leisurely fashion, and were concerned mainly with the influence of exteroceptive factors on the reproductive process—the theme of his Croonian lectures to the Royal Society in 1936. In his major work, *The Physiology of Reproduction*, published in 1910, he gathered together all relevant information about the breeding process in vertebrates and, to a lesser extent, in lower animals. This was rightly hailed as a masterpiece: a second edition appeared in 1922, and a third, largely rewritten by Marshall's colleagues and pupils, is now in the press. His awards included the Baly medal of the Royal College of Physicians (1935) and the Royal medal of the Royal Society (1940). At Cambridge he spent more than thirty-five years, first as lecturer and later as reader in agricultural physiology; at Christ's College he was successively tutor, dean, and vice-master. His colleagues knew him as a kindly and courteous man, shrewd and discriminating in judgment, willing to give full weight to another point of view and yet always getting to the core of the matter. Biology has lost one of its outstanding characters.

Prof. J. R. LEARMONTH has been appointed a surgeon to the King. Professor Learmonth, who is surgeon to the King's household in Scotland, has been attending His Majesty during his illness.

Dr. F. J. H. COUTTS, C.B., late senior medical officer, Ministry of Health, died in Bournemouth on Feb. 13 at the age of 83.

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The Wider World

NUTRITION AND HEALTH OF CHILDREN IN FIVE COUNTRIES OF SOUTH AMERICA

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2. Chile

WHEREAS Paraguay can properly be compared and contrasted with the State of an Indian Rajah, Chile must be judged against different standards. Scotland is a country with which Chile has much in common. Today each contains about 5 million inhabitants, of whom just under half live in the large towns. Each has rich agricultural lands and large mineral resources. In both there are vast bleak areas, stretching towards the Poles, where shepherds and fishermen struggle with a hard environment. Each country has grown up in comparative isolation from the main continent to which it belongs, and this has resulted in a keen nationalism and hardy individuality. The traveller from Edinburgh, waking in his hotel in Santiago and looking out of the window, will see faintly, through a thick haze of domestic and industrial smoke, the snow on the nearby hills, and may well for a moment think he is back in "Auld Reekie."

Except for a small area in the north, Chile is free from tropical diseases. Her Indian population is only 70,000, and most of these live in a reserve. The overwhelming majority of her inhabitants are European. Her methods of agriculture and industry are essentially European, and her health records must be considered in relation to the best standards of the European peoples.

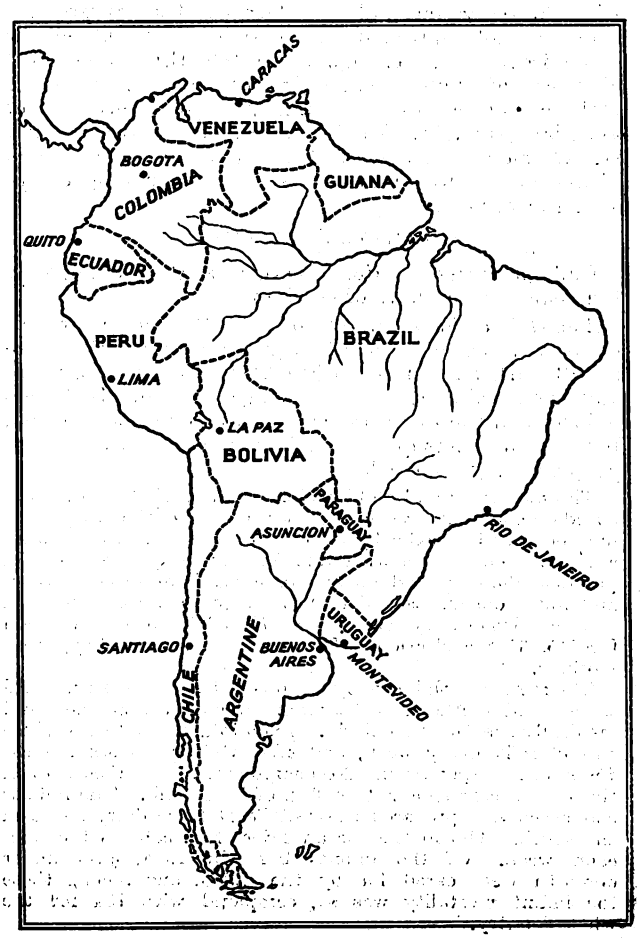
Medicine in Chile presents an interesting paradox. The visitor is immediately struck by the obvious skill and competence of the leading public-health authorities. They have evolved statistical information services, and vast systems of health legislation, which compare well with those of any country in the world. Yet their own figures show that in essentials they have, as yet, failed in their main purpose. A crude death-rate which fluctuates around 20, and an infant-mortality rate which has only recently fallen below 200, reflect the appalling condition of the people. Accurate information is available both about morbidity and mortality: Chile has the best bad health records in the world. The visitor must reflect on the possibility that had less time and money been spent on collecting information and planning comprehensive national health schemes, and more energy devoted to such mundane tasks as organising the milk and water supplies and sewage systems of small areas, the health of the people would have been better.

There are, however, two fundamental causes impeding progress in public health; a brief study of the industry and agriculture of the country shows essential weaknesses.

Chile's industrial wealth lies in her copper and her nitrate mines. These dominate all other forms of exportable wealth. Thus in 1939, out of total exports worth 138 million dollars, 38% was copper and 28% nitrates. These two commodities represent 66% of total trade. Chile's wealth has been thus utterly dependent on world prices for copper and nitrates. Industrially she has rested on an unsound basis. This instability has been aggravated by a tendency in good times for a large part of the wealth to be spent abroad. Conditions are altering now. Coalmines are being developed, and steel and light industries are starting. These should lead to an all-round economy and stability.

Agricultural statistics show that the over-all quantitative consumption of food is probably nearly adequate and there is no evidence of starvation or serious under-feeding. The gross defect is in the milk-supply, which corresponds to only 70 ml. per head per day for all classes. By contrast, the supplies of wines and spirits are double this amount, and Chilean wines are not weak—*experimentum feci*. All the persons with whom I discussed the matter confirmed this high alcohol consumption and very poor milk-supply. These two factors are largely responsible for the appalling health records. Alcoholism and a lack of milk lead to tuberculosis and dead babies as surely as night succeeds day.

Another vital factor is the housing condition of the people. Many thousands live huddled together in shacks which have been put together from scrap timber and corrugated iron. Their sanitary system is based on the open sewer and garbage pit; their water-supply is neither easily accessible nor safe. In comparing and contrasting slums, one thinks of Naples, of Glasgow, of Calcutta and Warsaw: even judged against these standards of squalor and human wretchedness, some of the inhabitants of the municipality of San Miguel in Santiago city live under shameful conditions. The environment lacks the basic elements of human decency. In the municipality of Cuinto Normal, which superficially looks infinitely better than San Miguel, a recent survey has shown 4·5 persons per room (including kitchen) and just over 2 persons per bed. The visitor to Santiago sees great building activities: huge government offices, luxury hotels, large blocks of modern luxury flats, modern hospitals and laboratories, a magnificent sports stadium—all these are being, or have lately been, erected. But there is little sign of the construction of workers' dwellings.



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VITAL STATISTICS AND HEALTH RECORDS

The accompanying table gives a few basic facts set beside similar ones for Scotland.

	Chile (1944)	*Scotland (1945)*
Population	5,272,784	4,673,900
Birth-rate per 1000	33·2	16·9
Death-rate per 1000	19·5	13·2
Infant-mortality rate	181·0	56·0
Stillbirth-rate	40·0	32·8
Maternal deaths (rate per 1000 births)	6·2	2·8

PRINCIPAL CAUSES OF DEATH (% OF TOTAL DEATHS)

Pneumonia	18·6	3·5
Heart diseases	10·2	28·2
Diseases peculiar to the first year of life	10·0	3·2
Pulmonary tuberculosis	9·6	4·5
Diarrhœa and enteritis	8·4	1·6
Cancer	4·0	14·8
Violence	3·9	4·7
Simple meningitis (infantile convulsions)	2·7	less than 1
Cerebral hæmorrhage and embolism	2·5	11·6
Influenza	2·4	less than 1
Whooping-cough	1·6	,, ,, ,,
Maternal mortality	1·1	,, ,, ,,
Nephritis	1·0	1·9
All other causes	24·1	26·0

These figures demonstrate the heavy mortality from pneumonia and tuberculosis and in young children. Nearly 43% of all deaths are recorded as occurring before school age.

The principal causes of infant deaths are pneumonia, congenital debility, diarrhœa, and enteritis, convulsions, and premature births, which in 1944 accounted for 23,267 deaths, or 73% of the total. Corresponding figures for Scotland are 3057 and 63%. There is no doubt that poor nutrition, both of the expectant and nursing mothers and of the recently weaned infant, predisposes to these many deaths.

It is the high death-rates that afford the main evidence of malnutrition in Chile. Deficiency diseases are not common, and I saw no definite case in any of the schools or clinics visited. Though I was told that radiological evidence of mild rickets is not uncommon, gross rachitic deformities are rare, no doubt because of abundant sunlight. Dental caries, on the other hand, is extremely common, and the children in a school visited in San Miguel had worse teeth than I remember seeing anywhere.

CHILDREN'S SERVICES

Chile possesses a variety of organisations looking after the health and welfare of children.

The *Caja de Seguro Obligatorio* (C.S.O.) aims at providing a comprehensive health service and social insurance for all workers, and also a health service for their wives and their children up to the age of two. It covers industrial and agricultural workers and domestic servants, but large numbers of casual labourers and many indigent people are not included.

The maternity and child-welfare services of the C.S.O. are based on health centres or consultarios. Here the prospective mother may be medically examined: she can also have an extensive course in mothercraft from trained nurses, and in practical dietetics and home economics from social workers and nutritionists. She does not receive any extra food in these centres or elsewhere. In 1947, 55,307 mothers attended for 245,037 consultations. This represents about 30% of all mothers.

The mother with her baby attends at the centre for medical advice and mothercraft training. Babies are weighed and medically examined regularly. Each infant gets two or three tins of milk every week, and after the age of six months 250 g. of flour per week. No charge is made for these. Each tin of milk corresponds to 450 g. of fresh milk. The milk is condensed and prepared by Nestlé's at large dairy-farms in the south. The mother or an elder child collects the milk each week. Of the infants born in 1944, just under one-fifth were cared for by the C.S.O. and among these the infant mortality was 93, compared with 184 for the whole country.

I was able to visit two foster-homes, in each of which three infants, whose mothers were in sanatoria suffering from pulmonary tuberculosis, were receiving care. The homes were ideal and in each case the C.S.O. supervised the foster-mother, who received money, food, and equipment. The very competent social worker who showed me these two homes said that only a few were available, but their very existence shows the high aims and ambitions of the C.S.O.

The *Direccion General de Protección a la Infancia y Adolescencia* (D.G.P.I.A.) is a complex government organisation which provides a variety of services. It has 35 maternal and child-welfare centres. At these, in 1947, there attended 13,304 prospective mothers, 11,816 infants under two years, and 12,048 preschool children. These mothers and children are mostly from the very poorest sections of the population and many are totally indigent. They are not covered by the C.S.O. For financial reasons, it was only possible to give 10% of the attending infants milk and flour, though it was estimated that 70% were in need.

The D.G.P.I.A. is also responsible for the school medical service. This is run by 180 part-time doctors, who work two hours a day. In 1947 just over 200,000 school-children (about one-fifth of all children of school age) were medically examined. Of these 40% were regarded as undernourished, mostly because their height and weight were below accepted standards. Some 200,000 children receive milk in schools (about 200 ml. daily for five days a week). The milk is pasteurised in bulk and sent to the schools in drums for distribution. With it a small bun is sometimes provided. Only the poorest schools receive milk, and it is given free.

The D.G.P.I.A. is responsible too for a dental service at schools and centres, which were attended in 1947 by over 300,000 mothers and children, and a central children's psychiatric clinic, which saw 883 patients in 1947. It administers six homes for juvenile delinquents, with accommodation for 1495 children.

In the C.S.O. and the D.G.P.I.A., Chile has two government organisations which provide excellent facilities for part of the child population. Some of the centres that I saw were models of their kind. They were staffed by efficient pædiatricians, social workers, and nutritionists. Emphasis was put on health education. The infants and children attending these centres would bear comparison with children anywhere. However, large numbers of the children grow up without the opportunity to benefit from these government services, which as yet only exist in miniature.

Private organisations have made notable efforts to fill part of the huge gaps, but in the time available I was unable to see any of their work.

CONCLUSION

Chile is attempting a vast experiment to accelerate and compress the normal development of her public-health services. Thus there are health centres, maternal and child-welfare services, tuberculosis services, health education programmes, and social security services that compare well with those of any other country. It is possible to see all these in operation, though the Chileans themselves admit that, so far, they cover only a small proportion of the population. The visitor must, however, ponder the efficacy of introducing these elaborate and expensive schemes into a country where the majority of the inhabitants have no suitable milk-supply and many live under shocking housing conditions with no proper water-supply and no sewage systems. The very high death-rates and the enormous toll of infant and preschool life add weight to these doubts, though it must be admitted that the last five years have shown an encouraging improvement in many health records.

Chile has a wealth of agricultural and mineral resources and clearly a great amount of medical talent, notably

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in public health. The solution of her manifold problems must be internal, and can depend to only a very small extent on aid from outside.

In a small country, it is inevitable that most of the leaders of the medical profession should go abroad for postgraduate training, and almost all the public-health workers I met had been in the United States for long periods. In this field of knowledge, the U.S.A. is at the moment practically the only training-ground. This is unfortunate. It has resulted in an almost total ignorance of the food policies and programmes of Great Britain and their relation to public health. A great deal of this is directly relevant to Chile. Many of the men with whom I talked were much interested in Britain's experiences; indeed, a lot of my time was taken up in discussing and explaining our policies.

It would clearly be advantageous to Chile if a proportion of her postgraduate students in public health came to Britain. Our problems are in most respects essentially the same, and we too could learn from her.

Public Health

Housing

CIVILISED society has to spend a great deal of time in taking stock. We must constantly review our various public services to see where they need reforming, and spend much thought besides on things which are partly in the hands of private enterprise. Housing is in the second class, and, as P.E.P. have lately pointed out,[1] we know very little about it. "Except in particular districts where special surveys have been made, nobody knows how many and what kind of households make up the demand. Not even the total number of dwellings in England and Wales is known, still less their types, sizes and rents or what size families live in what size houses." It is wasteful, P.E.P. point out, to use money, men, and materials in building houses larger than are needed, or in places where they are not wanted, or even possibly (for the population is declining) in greater numbers than can be used. It should be possible, they believe, to estimate housing needs fairly correctly.

Existing estimates have been based on the 1931 Housing Census, modified by assumptions about subsequent trends, on national sample surveys, and on local sample surveys. The 1931 census findings are out of date for various reasons: the analysis was not detailed enough, it was not made clear what was meant by the terms "families," "households," and "dwellings," and social developments since that time have invalidated the conclusions drawn. Nowadays more single people, widows, and old-age pensioners live independently, and families are smaller; so the general demand is for small dwellings. Sample surveys on a national scale also have their sources of error, for the districts chosen greatly influence the results, and a 5% error, when translated into national terms, may make a difference of half a million households either way—or in other terms, a three years' building programme at the present rate. However, national surveys and detailed local surveys are both useful in indicating social trends. P.E.P. suggest that all studies made—whether by census, sample surveys, or local inquiries into overcrowding, insanitary property, war damage, or housing waiting-lists—should be designed so that their results are comparable: thus a picture of the whole position could gradually be built up. They outline the sort of information needed: the number of married couples living together in the area surveyed; the size of the family; the age of the parents (from which it can be inferred whether the family is likely to grow or not); the occupation of the father (from which the size and type of home needed can be judged); the number of families which have their own homes; the number for whom the house is either too small or too large; the number of families sharing homes; and the proportion of overcrowded homes. At present we do not know accurately even the quantity of dwellings available, much less their quality, sizes, and types.

A housing census is needed to establish the facts; but as the material thus obtained would take some time to tabulate in full, P.E.P. propose that analyses should be made of samples of it: they believe that a complete analysis of a 5% sample would give a more accurate picture than did the isolated analyses, made in 1931, of Sheffield and Camberwell. Forecasts could then be made, based on demographic trends, and these could be checked by periodic national surveys. Since it is unlikely that a census would offer any useful material before 1952 or 1953, surveys by local authorities should be used to provide immediate data, and these should be collected in a comparable form. Indeed, local council records could be used at once if it were collated, and might suggest substantial economies in the housing programme.

1. Planning. Jan. 10, 1949. From Political and Economic Planning, 16, Queen Anne's Gate, London, S.W.1.

Influenza

There was a rise in deaths in the great towns from 37 in the week ended Jan. 29 to 64 in the week ended Feb. 5, but this is not a high figure in comparison with that in the corresponding week of any previous year except 1948. There has been a definite increase in the number and size of outbreaks reported from residential schools, Service establishments, and so on; but in all outbreaks the disease appears to be relatively mild and short-lived. Outbreaks are widely scattered.

International Situation.—In France the epidemic is on the wane, but in some regions a slightly higher proportion of serious cases is being reported than in the earlier stages of the epidemic.

Notification of Infectious Diseases

ENGLAND AND WALES

—	Week ended Jan.				
	1	8	15	22	29
Cerebrospinal fever	28	43	28	24	45
Diphtheria	142	126	92	131	141
Dysentery	53	81	70	104	60
Encephalitis lethargica	..	..	2	1	..
Food-poisoning		19	19	112	50
Measles, excluding rubella	11,165	13,210	10,996	10,258	11,657
Ophthalmia neonatorum	48	50	48	39	56
Paratyphoid fever	3	2	4	1	2
Pneumonia, primary or influenzal	1051	1186	1189	1053	935
Polioencephalitis	3	1	3	2	1
Poliomyelitis	20	19	34	26	20
Puerperal pyrexia	66	73	88	96	89
Scarlet fever	1126	1023	1000	1314	1191
Smallpox	..	..	..	..	..
Typhoid fever	7	4	5	3	3
Whooping-cough	2018	2314	2828	2942	2857

"... We have a tendency to interpret life, not as it really is, but in the light of our own ideas. We seldom think that some of our present ideas may be wrong and will change with the passage of time. Thirty years ago 'painted women' and prostitutes were synonymous terms; today the unpainted woman is a rarity. An immoral slum girl is a harlot; an immoral society lass 'has a good time.' A 'scrounger' in the army, souvenir hunters in hotels, those who evade taxation, tram fares and other legal charges, are not stealing. They are simply doing what everyone else is doing. But the boy who steals fruit or money to pay his fare to a distant city, which he has an irresistible desire to see, is a delinquent child to be reformed at all costs. La Fontaine's fable of the lion and the ass is still true to life."—Dr. S. J. MINOGUE, *Med. J. Aust.* Jan 29. p. 130.

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Special Articles

MENTAL-HOSPITAL TREATMENT OF DEPRESSION

BY A FORMER PATIENT

THE lapse of over two years since, after a six weeks' stay as a voluntary patient, I discharged myself from one of the leading mental hospitals, has, I hope, made it possible to record objectively both the virtues and shortcomings of this environment in the treatment of depression.

At the age of 50 the breakdown of a long-standing but unsuspected pulmonary tuberculous lesion, after six war years of extra strain and work, necessitated six months' hospital and sanatorium treatment. This was very successful and was accompanied by marked gain in weight, mental relaxation, and a sense of well-being. The return from sheltered sanatorium routine to ordinary surroundings and responsibilities was, however, rapidly followed by deep depression accompanied by intractable insomnia. As much for the sake of my family as for myself, it seemed essential that I should receive some form of institutional treatment; and after some preliminary observation and unsuccessful sedation I agreed to enter a mental hospital.

ADMISSION

The incidentals attached to admission to this type of hospital are distressing to an already depressed patient, but are probably unavoidable. They include the deprivation of *all* personal belongings (not only such potentially lethal weapons as nail-scissors and a cigarette lighter); the discovery that one is expected to eat with cutlery specially constructed to be incapable of causing any wound; and similar ostentatious curtailments of elementary individual privacy and liberty. It is questionable, however, whether it is absolutely necessary to house the newly admitted depressed patient, who may be regarded as still fundamentally sane although oppressed with fear for his own sanity, with the more macabre lunatics. It was perhaps peculiarly unfortunate that, owing to unrepaired war damage in this instance, new admissions were housed in the same block as, and directly over, the "refractory" cases, whose cries, accompanied by tattoos beaten on the doors, punctuated the night and were followed by unmistakable sounds of a scuffle and forcible "drenching" with paraldehyde or some other narcotic. This mixing of the relatively slightly ill with distressing cases of insanity (some of ten or more years' standing) also continued in the so-called "convalescent" block and certainly did not contribute to the peace of mind of the former class of patient. Most of the extremely chronic and severe cases of insanity seemed to be so completely shut off in their own world that it is doubtful whether they derived any benefit from mixing socially with the mild and relatively transient cases. The undoubted distress caused to the latter type of patient did not appear to be justified by any therapeutic gain.

INVESTIGATION

In view of my history of recent sanatorium treatment it was not unreasonable to expect some routine physical examination soon after admission. This was not made then or at any time during my stay; not even a blood-pressure reading was taken. On admission I was weighed in pyjamas on a spring balance and my temperature taken in the axilla; about a month later we were all weighed fully clothed on a different weighing-machine. Some investigations were made in the pathological laboratory: Wassermann and van den Bergh reactions, a complete blood-count, and possibly a routine urine examination. The blood-count had an amusing sequel, which was nevertheless somewhat disturbing to a depressed patient: a day or two later, in the course of one of the routine daily rounds, the medical officer asked if my previous blood-counts had been normal. On being told that they had he said, "Oh, that's all right. The lab. reported that you had a high colour-index. I expect their photometric colorimeter has gone wrong." Visions of the possible significance of a high C.I. were left to mature for nearly a week before a repeat test revealed a normal index.

Apart from ten minutes' conversation on the day of admission, there was nothing that could be called a psychological or psychiatric consultation until the last ten days of my stay, when a psychiatrist doing temporary holiday duty at the hospital devoted many hours a day to a selection of the patients in the convalescent block. Several of the patients, including myself, were deeply indebted to this visitor, who transformed our relatively hopeless outlook, and in my own case reinforced a wavering determination to seek another environment. Otherwise contact with the medical officers was limited to a very perfunctory daily round in which inquiries about one's state of health were made in the presence of other patients; it required, in fact, considerable manœuvring to secure even momentary privacy for a personal question and answer. These visits were often at meal-times when all the patients were seated at table and could not possibly seek any reassurance or personal advice. No routine consultations in any privacy were given. This contrasted very strongly with the ease with which personal advice could be obtained from medical officers in the sanatorium, and with the routine examinations and consultations given in privacy there. The staff of the sanatorium certainly had no less work to do than that of the mental hospital. Many patients were continually irritated by what appeared to them to be attempts to fob them off with an easy answer which would keep them quiet. Explanations were given for intercurrent physical symptoms which were quite unconvincing to me and for which I have been unable to obtain confirmation on subsequent inquiry. Patients were also convinced, with some justification, that misleading and unwarrantably reassuring bulletins were given to relatives.

TREATMENT

There appeared to be a surprising failure on the part of the medical staff to appreciate the nature of the anxiety and fears of many patients. One outstanding example will suffice.

I watched a young man who appeared to be convalescent suffer a schizophrenic relapse. The onset, which seemed to be precipitated by nothing more serious than a common cold, was preceded by three or four days of increasing anxiety mounting to terror. I did what I could to relieve his state by encouraging him to talk and by reassuring him as far as possible; but his condition seemed to be completely unnoticed by the staff. Finally I took it upon myself to call a medical officer's attention to what was happening. I realise that probably nothing could have been done to avert this relapse, but I think the terror might have been mitigated by the timely use of suitable sedatives.

Rochefoucauld says: "Il est facile de supporter les maux d'autrui," but this is not the right attitude for any member of the medical profession, least of all for those who specialise in psychological medicine; more than ordinary imaginative insight and sympathy is demanded of them.

So far as a patient could judge, if a case was not considered suitable for electric convulsive therapy (E.C.T.), insulin-shock treatment, or lobectomy, the only treatment was diurnal and nocturnal "dope" in the form of barbiturates or paraldehyde, with some use of amphetamine sulphate. Owing to my recent lung lesion I

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was spared the ordeal of E.C.T., and I cannot say that my observations of its effects on others made me regret this. I realise that there is considerable evidence in the literature that beneficial results are obtained from E.C.T., though recent correspondence suggests an acute division of opinion in the psychiatric world on the propriety of using this apparently quite empirical method of treatment. I can only report my observations on fellow-patients over a period of a little more than a month. Apart from the immediate dazing effect, it was difficult to detect any psychological improvement; some of the patients appeared to be definitely regressing. Furthermore, in this short period there were at least 4 quite serious traumatic accidents: 1 patient fractured either the spines or transverse processes of two thoracic vertebræ, and was later discharged in an exceedingly incapacitating plaster jacket; 3 patients seriously injured their shoulders or brachial plexus, with resulting pain and weakness which were not remedied by several weeks' treatment. I cannot express any opinion on the results of insulin-shock therapy, but it seemed that a great opportunity to investigate and interpret the dreams and other subjective mental symptoms of patients undergoing this treatment was missed.

RECREATION, EMPLOYMENT, AND FOOD

Social amenities, recreational facilities, and occupational therapy should surely have an important function in the treatment of psychological disorders. In this hospital the accommodation for individual patients was good, with adequately equipped single bedrooms, the privacy of which was only limited by the fact that the door could not be latched from the inside. The common-rooms were pleasantly furnished, except for a dearth of comfortable chairs (the upright wicker arm-chair is not restful) and the continuous operation of the wireless, which gave very poor reproduction and maddening distortion. (There should be at least one common-room in which no wireless, musical instrument, or noisy games such as billiards are allowed; otherwise patients who wish to read or want freedom from noise are forced to seek the solitude of their bedrooms.) The common-rooms were liberally supplied with pianos, billiards, and table-tennis tables, and facilities for playing cards. The hospital stood in extensive, attractive, and well-wooded grounds where it was possible to play tennis, croquet, and bowls; but little was done to encourage patients to play games or take part in organised tournaments. Unfortunately, too, only a very small proportion of the deck-chairs were serviceable for those who wished to sit outside and read, talk, or play such games as chess.

The library arrangements were deplorable, comparing most unfavourably with those at the sanatorium I had just left. The list of books included few that any intelligent patient would wish to read, and there was no direct access to the library; parcels of unselected books were distributed on fixed dates to the different blocks and withdrawn after a fixed period without regard to the convenience of patients who might be reading them. At the sanatorium there was a classified catalogue of the extremely well-stocked library; this was circulated so that patients in bed could make a list of their requirements, and books were exchanged for them by the convalescent "up" patients several times a week. This service was much appreciated by those in bed, and provided occupation for those who were more fortunate; a similar service in the mental hospital would have benefited both those patients whose movements were restricted, and the others through the opportunity to be of service.

An occupational-therapy department existed; but its activities badly needed extending, and its services should have been available throughout the day instead of for about one hour in the morning and another in the afternoon. Manual activities such as leather-work, rug-making, weaving, and sewing appeal only to a small proportion of patients; pursuits providing greater mental occupation should be developed. Materials for modelling and painting were to be had, but little guidance or encouragement was provided and the occupations were not brought to the patients who, in view of their disability, required encouragement. In a mental hospital, occupational therapy suited to the individual patient should be a definite part of treatment; and, as in many sanatoria, patients should be employed as much as possible in helping to run the institution. Assisting with the indoor "chores" and with the work in the vegetable and other gardens would help to restore the patient's self-respect. Much more could be done to organise film shows, discussions, debates and "brains trusts"; a sufficient proportion of patients were well enough to take part in arranging these activities as they do in sanatoria.

OTHER OBSERVATIONS

Regular motor-coach excursions were provided into the surrounding country, but many patients were not attracted by the prospect of being driven round the countryside with "a coach-load of lunatics." Many of the patients were allowed out during the afternoon, usually on "accompanied parole," but this privilege had to be applied for in writing. If the confidence of the patients is to be retained, any letters addressed by them to the medical superintendent should be answered; in my own case an application to be allowed out "on parole" was not answered and it was only several days later that I heard indirectly through a male nurse that my request had not been granted.

The food was adequate, although in quantity, quality, and cooking it compared unfavourably with the hospital and sanatorium that I had been in during the previous six months. It should surely be possible to arrange that patients entitled to supplements, such as extra milk, do in fact receive these, and that all receive enough of the accessory food factors. It seems to me that in a mental institution no less than in a Lyons Corner House the buying, cooking, and presentation of food should be supervised by trained experts. This is very rarely the case. There seems to be a lingering prejudice that attractive food is a gross indulgence of the flesh.

STAFFING

It would be wrong to end without paying tribute to the patience, sympathy, and skill of the male nurses; their persistent good humour and understanding when dealing with an exceptionally trying type of patient was beyond praise. This was all the more surprising since it did not appear that as a group they had been subject to any special form of selection. So far as my limited observation went, the same tribute could not be paid to the female nurses. This difference may be explained by the fact that the men regard their work as the occupation of a life-time, ending in a pension, and that most of them have wives and families to support.

Quite obviously medical officers in mental hospitals have difficulties from shortage of staff. Is this shortage unavoidable, however, and is it the whole explanation? The hospital concerned was a rich foundation and the patients paid for accommodation and treatment. Could not a larger staff have been employed if the authorities concerned really believed in the importance of individual psychiatric treatment? There were and are many medical men anxious to extend their psychiatric experience gained in the Forces during the war. It was difficult to avoid the suspicion that the medical staff were imbued with the classical "lunatic asylum" attitude to their job and were not interested in developing

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their limited opportunities for an analytic approach. It is to be hoped that the formation of an Institute of Psychiatry and the inauguration of the National Health Service will cause a revolution in the institutional treatment of mental disease and will provide some of those advantages that are now available only to the patient who can afford treatment in a private consulting-room. I think that meanwhile the institutional treatment of depression should be reserved for those who are completely incapacitated by their affliction or who are suicidal; difficult and painful as it may be, the others should make every possible effort to carry on with work and seek treatment either by private consultations or in an outpatient clinic. In my own case, I have learnt that adequate diurnal dosage with 'Sodium amytal,' combined when necessary with amphetamine sulphate and with paraldehyde at night, would have tided me over the worst period until psychiatric treatment enabled me to gain sufficient control to carry on with something approaching a normal life.

I left the sanatorium with a greatly enhanced respect for those engaged in the active treatment of tuberculosis and with an appreciation for the environment they created by their energy and sympathy. When every allowance is made for the sympathy and skill of the male nurses and the difficulties due to shortage of qualified staff, my experience does not allow me to feel equal confidence in those in charge of at least one mental hospital.

SCOTTISH HEALTH ADVISORY COMMITTEES

MEMBERSHIP of nine standing advisory committees, whose duty it will be to advise Mr. Arthur Woodburn, Secretary of State for Scotland, and the Health Services Council on various aspects of the National Health Service, is announced this week. The committees will advise on the Health Service matters with which they are concerned, both as they think fit and also on questions referred to them by the Secretary of State. They will report direct to the Secretary of State, but are required to inform the Health Services Council, who may express their views on the matter under consideration. Each committee consists partly of persons appointed by the Secretary of State after consultation with various representative organisations [listed under (*a*)], and partly of members of the Health Services Council appointed by the council [listed under (*b*)].

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(*a*) Dr. D. P. Cuthbertson, Prof. T. J. Mackie, M.D.

(*b*) Prof. Dugald Baird, F.R.C.O.G., Dr. A. D. Briggs, Prof. D. F. Cappell, M.D., Dr. W. G. Clark, Dr. Mary Esslemont, Prof. G. B. Fleming, F.R.F.P.S.G., Dr. G. M. Fyfe, J. M. Graham, F.R.C.S.E., Sir David Henderson, F.R.C.P., Dr. J. R. Langmuir, Prof. J. R. Learmonth, F.R.C.S.E., Dr. G. MacFeat, Dr. I. H. Maciver, Prof. J. W. McNee, F.R.C.P., Dr. A. F. Wilkie Millar, Prof. T. Ferguson Rodger, F.R.C.P.E., Dr. W. D. D. Small, Sir Sydney Smith, F.R.C.P.E.

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(*b*) Dr. R. C. Scott Dow, J. F. Henderson, Thomas Rankin, L.D.S.

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(*b*) Miss J. P. Ferlie, Miss C. M. Keachie, Miss E. G. Manners.

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(*b*) C. G. Drummond, M.P.S., Dr. D. McCall.

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(*a*) Dr. R. Bailey, J. Brownlee, F.H.A., James McKelvie, J. MacKenzie, Miss Eleanor Stewart, Russell Paton.

(*b*) Prof. Dugald Baird, Dr. A. D. Briggs, Prof. D. F. Cappell, Dr. R. C. Scott Dow, Lieut.-Colonel J. C. Dundas, Dr. Mary Esslemont, W. F. Ferguson, F.H.A., Prof. G. B. Fleming, J. M. Graham, F.R.C.S.E., Sir David Henderson, Prof. J. R. Learmonth, Sir H. Broun Lindsay, Dr. D. McCall, Dr. G. MacFeat, Prof. J. W. McNee, Miss E. G. Manners, Prof. T. Ferguson Rodger, Dr. W. D. D. Small, Sir Sydney Smith, Captain Joseph Steel, Captain J. P. Younger.

LOCAL-AUTHORITY SERVICES COMMITTEE

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(*b*) Dr. W. G. Clark, Alexander Cunningham, Miss J. P. Ferlie, Dr. G. Matthew Fyfe, J. F. Henderson, Miss C. Keachie, Sir H. Broun Lindsay, John Mann, William O'Neill, Prof. T. Ferguson Rodger, Captain Joseph Steel, Provost James Young.

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COMMITTEE ON HEALTH SERVICES IN THE HIGHLANDS AND ISLANDS

(*a*) Dr. J. R. Anderson, J. S. Banks, Dr. W. N. Gray, A. J. C. Hamilton, F.R.C.S., Dr. J. L. Horne, Provost A. J. Mackenzie, Dr. A. J. Macleod, Ian McClure, F.R.C.S.E., Councillor Donald Macpherson, Provost Hugh Ross.

(*b*) Dr. I. H. Maciver.

HEALTH-CENTRES COMMITTEE

(*a*) Councillor W. P. Earsman, Dr. D. Dale Logan, Dr. John Winning.

(*b*) Dr. W. G. Clark, C. G. Drummond, M.P.S.; Miss C. Keachie; Prof. J. R. Learmonth, John Mann, Dr. A. F. Wilkie Millar, Thomas Rankin, Dr. W. D. D. Small, Sir Sydney Smith.

WORLD HEALTH ORGANISATION

SINCE last September, when W.H.O. was established as a specialised agency of the United Nations, the staff has been increased to 254, of whom 194 are employed at the headquarters in Geneva, 29 in New York, and 32 in the field. Dr. Brock Chisholm (Canada) is the director-general of the organisation and Dr. W. P. Forrest (U.K.) his special assistant. The staff now includes the following:

Department of Technical Services

Director.—Dr. R. Gautier (Switzerland), assistant director-general of W.H.O.

DIVISION OF EPIDEMIOLOGY

Director.—Dr. Y. Biraud (France).

Section of Epidemiological Statistics and Information.—Dr. M. Cakrtova (Czechoslovakia).

Sanitary Conventions and Quarantine.—Dr. G. Stuart (U.K.) and Mr. G. de Brancion (France).

Studies of Communicable Diseases.—Dr. M. Sidky (Egypt).

Technology.—Mr. Z. Deutschman (Poland).

Health Statistics.—Dr. M. Pascua (Spain).

Therapeutic Substances.—Mr. P. D. Blanc (Canada).

DIVISION OF EDITORIAL AND REFERENCE SERVICE

Director.—Dr. N. Howard-Jones (U.K.).

Editorial.—Dr. A. Manuila (Rumania).

Translation.—Mr. G. Meyer (France).

Publication.—Mr. L. Porte (Switzerland).

Library and Reference.—Dr. G. Genty (France).

Department of Operations

Director.—Dr. Neville Goodman (U.K.), acting assistant director-general of W.H.O.

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DIVISION OF FIELD OPERATIONS

Director.—Dr. Goodman.
Special Office for Europe.—Dr. Norman Begg (U.K.).
Fellowships.—Dr. J. Vesely (Czechoslovakia) and Dr. D. Messinezy (Greece).
Medical Supply.—Dr. C. Y. Shu (China).

DIVISION OF PLANNING

Director.—Dr. W. Bonne (Netherlands).
Malaria.—Dr. E. Pampana (Italy).
Tuberculosis.—Dr. J. B. McDougall (U.K.).
Mother and Child Health.—Dr. Cicely Williams (U.K.) and Dr. E. Leppo (Finland).
Venereal Diseases.—Dr. T. Guthe (Norway) and Dr. E. Cross (New Zealand).
Public Health Administration.—Dr. X. Leclainche (France) and Dr. E. Grzegorzewski (Poland).
Mental Health.—Dr. G. R. Hargreaves (U.K.).

Other Directors

ADMINISTRATION AND FINANCE

Director.—Mr. M. Siegel (U.S.A.).

LIAISON OFFICE IN NEW YORK

Director.—Dr. F. Calderone (U.S.A.).
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LEGAL SECTION

Director.—Mr. A. Zarb (France).

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Director.—Mr. J. Handler (U.S.A.).

REGIONAL OFFICE FOR SOUTH-EAST ASIA AT NEW DELHI

Director.—Dr. C. Mani (India).

EPIDEMIOLOGICAL INTELLIGENCE STATION AT SINGAPORE

Director.—Dr. P. M. Kaul (India).

EASTERN MEDITERRANEAN CONFERENCE

On Feb. 7 representatives from nearly 20 countries and territories met at Cairo in the first conference of the W.H.O. regional committee for the Eastern Mediterranean. Dr. Brock Chisholm, Dr. Neville Goodman, and Dr. W. P. Forrest attended the meeting, and Sir Aly Tewfik Shousha, Pasha, chairman of the W.H.O. executive board and Egyptian under-secretary of state for health, was also present.

The delegates accepted the Egyptian government's offer to provide accommodation for the new regional office in Alexandria. Dr. Goodman later outlined W.H.O.'s programme for 1949 for the Eastern Mediterranean region. This included sending demonstration teams or experts to Pakistan for malaria control, to Egypt and Pakistan for tuberculosis and maternal and child health, to Turkey and Egypt for venereal-disease control, and to Ethiopia for environmental sanitation and other public-health work. More than 30 fellowships will also be provided for doctors from these countries and Iran.

PALESTINE REFUGEES

Emergency plans to prevent outbreaks of epidemic diseases among the Palestine refugees are outlined in a preliminary report submitted by Dr. John Cottrell (New Zealand), who recently was appointed W.H.O.'s representative with United Nations Relief for Palestine Refugees.

Dr. Cottrell was appointed at the request of the International Committee of the Red Cross, the League of Red Cross Societies, and the American Friends Service Committee, the three voluntary agencies responsible for actual relief operations. He works closely with UNICEF, which is furnishing food and medical supplies on a large scale. W.H.O. has also lent Dr. J. Peterson (U.S.A.) as chief medical officer to the American Friends Service Committee, which operates in Southern Palestine. Dr. Peterson is the former chief of the W.H.O. mission in China.

Although no serious epidemic has yet occurred among the 600,000 to 800,000 refugees scattered through Lebanon, Transjordan, Syria, and Palestine, Dr. Cottrell points to potential threats from malaria, dysentery, typhus, and other communicable diseases. Most of the refugees are now collected into camps or living in towns and villages, though a few are still scattered over the countryside. Sanitation and rubbish disposal generally are bad and water-supplies insufficient. Work on emergency sanitation projects has begun in Lebanon camps and will soon be extended to other areas.

In England Now

A Running Commentary by Peripatetic Correspondents

What is the doctor? What veracious fan
Has accurately drawn the native man?
Angel of light, or devil black as mud?
True-blue as BROTHER JONATHAN or red as BLOOD?
Like SAWYER callous, LEVITT-like a friend?
Secure as PANGLOSS in a prosperous end?
Like WATSON, proud to share another's yield,
Or THORNDIKE, paramount in every field?
As COLLY RIDGEON, to the manner born?
PRUNESQUALOR-smooth, or blunt as DR. THORNE?
Supremely right, in MUNTHE's own conceit,
Or meanly wrong, as CRONIN saw the Street?

A SLOP for folly, or a FAUST for pride,
Sometimes a JEKYLL, oftener a HYDE,
The true apothecary, what is he? . . .
Since doctors differ, authors disagree.

* * *

Working now in a teaching hospital, where efficient ancillary services are all on tap and we count the anæsthetists as well as the swabs at the end of an operation, I find it strange to recall the conditions under which we used to work. I remember particularly one night soon after the end of the war—

I had just got an Army grading and had been posted to a C.C.S. in a remote part of Germany. I was nervous of having to deal with major surgical cases without an O.C. Division to send for if I got into difficulties. The first serious case to come in was a Belgian despatch-rider who had come off his motor cycle on a dark foggy November night. He was one of those patients whom you transfuse before examining. Signs of life were present, but the blood-pressure was unrecordable. We ran in two pints of plasma as quickly as possible and he improved greatly. He had grossly comminuted compound fractures of both upper and lower jaws, his left leg appeared to be amputated below the knee, and he had a simple fracture of the left ulna.

I asked for volunteer blood-donors and two stalwarts came forward. As soon as the first was pricked with the needle he fainted. I learned afterwards that he always did this, but it was disconcerting at the time. There could be no doubt that I was in the vein, but not a drop of blood would come. After ten minutes' fiddling around I discovered that the non-return valve in the taking set had been inserted the wrong way round.

The anæsthetic was the next problem. I went to ask the O.C., who was in bed, if he would come and dope for me. When he heard about the case he remembered that he was a gynæcologist and hadn't given an anæsthetic for seven years, so he ordered the psychiatrist (the only other doctor in the unit), who hadn't given one since he qualified, to perform. So we started. While I was scrubbing up, one of the orderlies thought that the blood should be running in more quickly, so he applied pressure with a Higginson's syringe. The result was disastrous. The bung flew out of the bottle, half a pint of good blood spattered over the floor, and the needle was ripped out of the vein. I asked the psychiatrist to put the drip up again, but he said that he had never done one before. By this time all the veins had collapsed, so to save further trouble I cut down on a vein in the good leg. With so much œdema and bleeding in the mouth we thought it would be safer if we did a tracheotomy to maintain the airway, so I did this—my first—under local. At last I was ready for the general anæsthetic and asked the psychiatrist to give 'Pentothal' into the blood drip. This seemed to be the method which I could supervise most easily. His idea of controlling the depth of anæsthesia was to count the respiration-rate. He sat with a syringe in one hand and a watch in the other—" one, two three, four, five . . ."

The leg was not so bad as it had seemed. Both bones and most of the soft tissues were divided just below the knee, but the vessels were intact. I did a little surgical toilet and applied a " Tobruk " plaster. Meanwhile an orderly had put a padded plaster on the ulna and our dentist had taken impressions for making dental splints. The patient's general condition was not at all bad, but we left him in the theatre for the rest of the night.

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Two days later we were able to fly him back to England, and a few months later I heard that he was still in hospital but doing well.

I wonder where he is now and whether he knows how many hazards he survived that night.

* * *

The casualty room was looking rather more gory than usual when I poked my head round the door the other day. "Come in, come in, you might as well," the casualty officer at the wash-basin hailed me grimly. "I've had half the neighbourhood milling around in here—relatives, police, reporters. Look at the state of the floor." There were bloody footprints everywhere. "The second attempted suicide this week," he explained, seeing my puzzled expression. "Old chap—used a cut-throat. The usual story; held his head right back, slashed across his larynx and neck muscles. All blood and froth; never touched the big vessels. The inefficiency of some people!" He finished scrubbing his nails and reached for a towel. "Some day," he continued, "I'm going to write a little book for the layman, something on the lines of *Suicide in Six Easy Lessons*. You know the sort of thing—diagrams of the main vessels; how to make a room airtight; the lethal doses of all the common disinfectants; coloured plates of Deadly Nightshade and poisonous fungi." He put on his jacket. "Another thing," he said feelingly, "the aspirin people ought to be compelled by law to label their bottles 'Nothing under *x* tablets guaranteed fatal.'"

* * *

My criticisms of clinical teaching are simple and could be corrected in the first week of any teachers' training course:

(1) They can't be heard.

(2) What they are doing can't be seen.

(3) They (so rightly) ask students questions and the students' answers can't be heard but the discourse goes on as if the rest of us weren't there.

The high-spot of (1) was when the chap who was advising us how to demonstrate cases in the theatre said "... and when you read the history speak up so that the fellows at the back can hear." His own technique is to be secret and confidential whenever he has something important to say. Apropos of (2), where is that much-advertised amplifying stethoscope with "teaching leads" used? Of (3) one can say that with bad luck the teacher will be sidetracked and the rest of us will spend the next ten minutes craning our necks for scraps of muffled conversation. I hasten to add that students are far more inaudible than teachers; but damn it, sir, we are usually awestruck or afraid of making fools of ourselves.

* * *

BALLADE OF GENERAL PRACTICE

I am an inoffensive sort of man
—Tho' won't admit I wouldn't hurt a fly—
My school reports said: "Does the best he can,
His maths are weak; he cannot mastre π.
Next term, perhaps, he'll have another try."
I pity fellow creatures in distress.
Their faces are so long and that is why
I do my best to work the N.H.S.

"Please, doctor, while you're here, see Maud and Stan;
And Uncle Fred wants something for his eye;
And please to call next door on Mr. Cann,
Who's never been himself since last July;
And Grandma's not particularly spry,
Please send her out a tonic ..." "Yes, yes, yes—"
I grit my teeth prepared to do or die.
I do my best to work the N.H.S.

At home waits Mrs. Jarvis with her clan,
And Mrs. Smith could never pass me by
Without a word about her pot-and-pan
(Meaning her husband) who is far too shy
To bother me himself since he went dry.
(I much preferred him drinking to excess
As, married to that woman, so should I.)
I do my best to work the N.H.S.

Envoi: Bevan, your overheads are rather high.
An extra 60 million (more or less).
Works out a shade expensive, don't it, Nye?
I wouldn't know. I work the N.H.S.

Letters to the Editor

THE FREEDMAN INHALER AND THE MIDWIVES

SIR,—In 1943 you published my account[1] of an inhaler designed to provide trichlorethylene-air analgesia in childbirth, and specially constructed to prevent the possibility of inducing anæsthesia. I hoped it could be safely placed in the hands of an unsupervised midwife for domiciliary work. A special committee appointed by the Royal College of Obstetricians and Gynæcologists to investigate the analgesic use of trichlorethylene has now reported,[2] and on its findings the council of the college declare themselves unable to recommend the inhaler as safe for use by unsupervised midwives. The report states that "further attempt is being made to produce an apparatus which may fulfil all the requirements for safety."

According to the report, eight of the observers held that trichlorethylene could be safely used by unsupervised midwives; two thought there was a danger that midwives might use it for longer periods than had been the case in the series studied, and that a slightly weaker mixture of trichlorethylene and air would be more satisfactory; while two observers were definitely against its use by unsupervised midwives—for reasons which were all negated by conclusions stated in the body of the report.

Dr. P. J. Helliwell and Dr. A. M. Sutton, who collated evidence and wrote the report, object to the inhaler because (they say) it delivers an inconstant trichlorethylene-air mixture. They fear that in conditions less ideal than those of hospital practice, or by deliberate misuse, variation might be greater, and the mother would pass beyond the stage of coöperative analgesia into a state of uncoöperative stupor. However, it will, I think, be generally conceded that with this inhaler stupor precedes anæsthesia, and in such an event it would be to the midwife's own interest to remove the inhaler while the mother is merely drowsy.

I do not believe it will be possible to produce an apparatus capable of giving adequate analgesia yet never causing anæsthesia in any circumstances. Any standard device giving satisfactory analgesia for the many will provide more than enough for a minute number who are susceptible, and misuse here may certainly lead to anæsthesia. The patients themselves vary far more in their susceptibility than does the strength of the vapour with this equipment; and in any case the vapour variations are within a narrow range. Moreover, the mother safeguards herself against overdose because, as the report points out, she uses the equipment less if she gets drowsy.

The findings of the committee overwhelmingly support the efficacy of trichlorethylene analgesia in childbirth.

In the opinion of the great majority of both mothers and observers the inhaler gave satisfactory relief. It was better than the Minnitt machine, and the duration of administration had no effect on its efficacy. The coöperation of a few patients was somewhat impaired by drowsiness, but delay in labour because of this was trivial. The forceps-rate and interference-rate were well within normal limits, and there was no adverse effect on the maternal-mortality rate. One observer was concerned about a few cases of slowing of the fœtal heart-rate, but in no case was any harm done; in fact, the incidence of asphyxia neonatorum, too, was well within normal limits. The rates for stillbirth and neonatal death were not increased.

Neither the council nor the committee explain clearly why they cannot recommend the inhaler as safe for use by unsupervised midwives. The objections raised by 2 of the 16 observers, and by the collators, can all be disputed, on evidence given in the report. The midwife already carries in her bag the means to induce anæsthesia if she chooses to misuse it. Now she is refused the use of a method which, as the committee show, gives better analgesia than gas-and-air, and also, possibly, a lower incidence of maternal mortality, asphyxia neonatorum, stillbirth, and neonatal death rates. If the inhaler is to

1. *Lancet*, 1943, ii, 696.
2. Royal College of Obstetricians and Gynæcologists, Ninetenth Annual Report, 1947.

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be withheld from a midwife on the grounds that, in the remote possibility of her inducing anæsthesia, a fatal accident might follow, then it can be argued that anæsthetics should never be given, since deaths have been known to occur even when qualified doctors give them. The only rational course would be to arrange an investigation, in domiciliary practice, to compare the inhaler with the methods now in use.

Hendon, N.W.4. A. FREEDMAN.

*** The college's report is reviewed on p. 312.—ED. L.

PALLIATIVE SURGERY IN FACIAL PALSY

SIR,—Before surgeons embark too enthusiastically on attempts to alleviate facial paralysis by fascial slings or nerve operation they should clearly appreciate certain facts regarding this lesion.

1. Complete unilateral facial paralysis is not always disfiguring with the face at rest: indeed the side of the paralysis may only become apparent on facial movement.

2. Some cases of facial palsy develop a disfiguring contracture of the paralysed side, a tendency which may be aggravated by the introduction of fascial slings.

3. Facial palsies whether from trauma or from Bell's palsy either begin to recover within three or four weeks with a perfect restoration of function, or they may recover slowly by nerve regeneration. A very small proportion remain permanently paralysed.

4. Some recovery of movement following nerve regeneration first becomes evident three to nine months after the palsy, and improvement continues for a year or longer.

5. If operations to "decompress" the facial nerve are to be advocated on the theory that the nerve is compressed, there are two rational alternatives: (*a*) one may either operate on all cases on the day the palsy develops, though this involves many unnecessary operations; or (*b*) the operation should be delayed for at least nine months after the palsy appears, that is until sufficient time has elapsed to ensure that good natural regeneration will not occur. Operations carried out within six months of the palsy appearing are therefore unreasonable, and reports of good results following intervention at this period are meaningless.

6. *Perfect* recovery of facial movement is impossible when regeneration of the nerve has to occur; the inevitable mass movements can be observed for the rest of the patient's life. There can therefore be no such thing as a "perfect recovery" after nerve suture.

7. There is room for further research on the natural history of facial palsy to provide a clear background with which to compare alleged improvements in treatment.

Oxford. W. RITCHIE RUSSELL.

HOSPITAL BIOCHEMISTS

SIR,—It appears from his letter of Feb. 5 that Dr. Taylor also regards the non-medical chemist (N.M.C.) as a technician; so the point at issue is whether a technician or a medical consultant should be in charge of the routine laboratory.

The investigation of a patient's sickness starts at the bedside and may continue into the laboratory, and the task of the laboratory is to give the necessary clues to the clinician as quickly as possible. The choice of investigation is determined by the history and condition of the patient, and it is at this point that the medical qualification is desirable—it does not matter whether the laboratory consultant is called a chemical pathologist, clinical pathologist, biochemist, or physician for metabolic disease. I cannot too strongly condemn the idea that all tests must be completed before they are reviewed, for this leads straight to penny-in-the-slot pathology and a great increase in laboratory output, usually without corresponding benefit to the patient; while the clinician is tempted to use laboratory tests to replace careful clinical observation. On the contrary, the results of one test should be used to indicate whether further tests are desirable, and if so, which test is to be performed next. If the results are "coloured" by this procedure —i.e., falsified to agree with preconceived ideas—then the analyst is fundamentally dishonest and has no business to hold any responsible position. A N.M.C. of marked personality can sometimes overbear even an experienced clinician, and I have seen gross errors of diagnosis made in this way: he is an expert technician, but should lean on the morbid physiologist, and is therefore an assistant rather than a principal.

Finally, all laboratory workers—and consultants generally—are eccentrics who take up their specialised work because they enjoy it. The course in chemistry given to medical students is an excellent introduction, and it should not take long for an eccentric interested in medical chemistry to turn himself into a competent chemist—even though the average student fails to profit from that same course.

Central Middlesex Hospital, London, N.W.10. GEORGE DISCOMBE.

ESTIMATION OF BASAL METABOLIC RATE

SIR,—On Jan. 22 you published an article by Dr. Bene in which he claimed that the B.M.R. could be calculated by multiplying the patient's respiratory rate by his pulse-rate and expressing the figure thus obtained as an index "—e.g., normal pulse-rate (72) × normal respiration-rate (18) = 1296. The normal range is 1100–1500." Some obvious criticisms of this paper sprang immediately to mind. (The figures for the R.P. index which follow are expressed as a percentage, taking 1296 as normal.)

1. It is extremely improbable that so complicated a function could be expressed by so simple a formula, and previous methods such as those of Boothby and of Reid have, as Dr. Bene admits, proved completely fallacious.

2. Thyrotoxicosis is a disease of the whole body, but the parts of the body are unequally attacked. In different patients the assault is concentrated on different objectives. In some the most obvious results are mental, in others neurological, cardiac, respiratory, and so on. Neither the pulse-rate nor the respiratory rate bears any constant relationship to the severity of the disease or to the B.M.R. Thus one patient whose records I have re-examined in the past week had obvious clinical thyrotoxicosis and a B.M.R. of + 20·5 before thyroidectomy, but his respiration-rate at rest was 7 and his pulse-rate 82. After operation his B.M.R. was — 10, his respiration-rate was 8, and his pulse-rate 68. By Dr. Bene's method the B.M.R. works out at — 56% before operation and — 58% afterwards.

3. Dr. Bene claims that his R.P. index corresponded with the B.M.R. in 67% of 43 patients whose B.M.R. lay above + 15%, in 70% of 48 with a B.M.R. between + 15 and — 10%, and in 70% of 9 patients with a B.M.R. of less than — 10%. But he does not explain what he means by "correspondence"; he can hardly mean that it is exact. Within what range does he allow variation to occur without "correspondence" being vitiated?

4. He obtains his patients' pulse and respiratory rates after only 5 minutes' rest. This is not long enough for the truly basal values to be attained. So short a period of rest may be sufficient for a few; others require a little longer, and others again much longer. It follows from this that the figures for one patient are not comparable with those for another and that if his method is accurate for some it is bound to be inaccurate for others.

But, Sir, if despite these criticisms, Dr. Bene's method should work, it would effect an important saving of time and money. If it should not, it is important that his statements should, lest they prove a stumbling-block, be refuted at the earliest possible moment, for unfortunately a refutation never quite catches a fallacy, however hot it may follow on its heels. I therefore examined the records of 100 B.M.R. determinations performed on 87 unselected patients by Miss E. M. Dean in this clinic. To give Dr. Bene's method every chance I have allowed that the R.P. index corresponds with the B.M.R. when it lies within 10% of it in either direction, which I think is rather generous. I found that among 59 patients with B.M.R.s above + 15% there were 11 (19%) agreements, among 37 with B.M.R.s between + 15% and — 10% there were 3 (8%) agreements, and among—unfortunately—only 4 with B.M.R.s below — 10% there was 1 agreement. The disagreement was often profound. For instance, in one instance the B.M.R. was + 74% and the R.P. index — 22% and in another the B.M.R. was — 5% and the R.P. index + 46%.

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It may be argued that my figures are not strictly comparable with those of Dr. Bene because my patients had been at rest for several hours and his for only five minutes. There is justice in this argument, but it weights the scales against Dr. Bene. As I have pointed out, his figures cannot be equally accurate because his data are not equally basal (and it is the basal metabolism he seeks to estimate). But supposing they were equally accurate, one would expect them to give figures higher than mine because his conditions are less basal. The fact that the R.P. index is in 60% of my cases lower than the B.M.R. provides a final proof of my assertions that the two are completely unrelated to one another.

Thyroid Clinic, New End Hospital, London, N.W.3. RAYMOND GREENE.

SIR,—There are four standard methods for estimating the basal metabolism, and these depend upon measuring:

1. The heat output.
2. The oxygen consumption.
3. The carbon-dioxide output.
4. Both the oxygen consumption and the carbon-dioxide output.

For many years now, formulæ have been proposed for translating simple bedside records into an approximate figure for the basal metabolism.[1] These formulæ, like Dr. Bene's, are based on the fact that in thyrotoxicosis there may be tachycardia, an increased respiration-rate, and a rise in pulse pressure, whereas in hypothyroidism there may be the converse, and in normal people there may be more of these. The normal range of pulse-rate, respiration-rate, and pulse pressure is very wide, and, as they are not always greatly altered in thyrotoxicosis and in hypothyroidism, it is doubtful whether any of the formulæ can serve as a substitute for direct measurement of the basal metabolism. They may nevertheless have a certain clinical value: for example, the product of the pulse and respiration rates may well fall when thyrotoxicosis is reduced and rise when hypothyroidism is relieved.

For basal metabolism, the range accepted as normal is wide. Indeed, the range accepted by Miss Lovell and Dr. Martin is different from my own, based on a study of some 2300 people of both sexes from the ages of three to eighty. This makes the interpretation of the basal rate at times not easy, and on occasions erroneous. Severe thyrotoxicosis or hypothyroidism may be easy to diagnose clinically, and in these cases the basal metabolism is usually well outside the normal range; on the other hand, in the very mild cases, where assistance in the diagnosis may be most required, an isolated reading of the basal metabolism is of limited value.[2] Observations on the *variations* in the basal metabolism can be made a most sensitive index of thyroid dysfunction if:

1. *In the diagnosis of thyrotoxicosis*, the basal rate is measured before and after twelve days of iodine medication. Only in thyrotoxicosis does iodine cause a significant alteration in the basal metabolism.

2. *In the diagnosis of hypothyroidism* the basal metabolism is measured before and after two to four weeks of thyroid 2 grains daily. Only in hypothyroidism does thyroid medication in such doses and over such a period cause a significant rise in the basal rate.

Returning to Lovell and Martin's criticism of Bene's R.P. index, it appears possible that they may not have repeated quite accurately Bene's observations. Bene counted the pulse and respirations after a rest of only five minutes, whereas basal conditions require a rest period of at least thirty minutes. As Lovell and Martin referred to 50 unselected cases from their records, no doubt the respirations and pulses were recorded under basal conditions. It is no criticism of Bene's work that he chose arbitrarily a period of five, and not ten, twenty, or thirty minutes, for in seeking to make an intelligent guess at the basal metabolism, by a formula in no way related to heat output, it is not essential to comply with standard heat-output conditions. If he could devise the perfect formula by making certain observations while patients were standing on their heads, then all the more credit to Dr. Bene.

1. E.g., Read, J. M. *J. Amer. med. Ass.* 1922, **78**, 1887. Gale, A.M., Gale, C. H. *Lancet*, 1931, i, 1287. Jenkins, R. L. *Arch. intern. Med.* 1932, **49**, 188.
2. Robertson, J. D. *Lancet*, 1934, ii, 1076; *Ann. Surg.* 1949, **4**, 3.

In summary I think it can be said that the pulse-respiration product after a five-minute rest period may well have a certain clinical value, provided a correlation with the basal metabolism is not attempted.

J. DOUGLAS ROBERTSON.
Department of Clinical Investigation, The London Clinic, W.1.

SENIORS AND JUNIORS

SIR,—I have read with astonishment "Physician's" letter in your last issue. He states that the assessing committees appointed to advise the regional hospital boards on the status of consultant staffs are instructed to relegate junior consultants to a new category of "senior hospital officer." Last June the Minister of Health announced that the Government accepted in principle the recommendations of the Spens Committee. There is no doubt that the creation of a new barrier between the training of a specialist and the realisation of specialist status is a complete denial of the principles enunciated by the Spens Committee on this matter. It is dreadful to think that a decision of such importance to so many specialists can be taken in camera, especially when that decision is a categorical contradiction of an accepted principle.

Perhaps "Physician" is misinformed; but if he is not, then I hope this violation of principle will be actively resisted by such bodies as represent us.

SECOND PHYSICIAN.

MEDICAL TECHNOLOGY IN BRITAIN AND AMERICA

SIR,—Dr. Whitehead's article in your issue of Jan. 15 has been read with great interest by medical and scientific laboratory technicians throughout this country. Dr. Whitehead is to be congratulated upon his comprehensive survey of the position, particularly with reference to the training of those technicians who are eligible for membership of the Institute of Medical Laboratory Technology.

In discussing the work of technicians in anatomy and physiology and of those who are associated with science rather than medicine, he suggests that the formation of an independent association of these technicians might prove a satisfactory arrangement. The majority of those concerned are of the same opinion, and I am sure that Dr. Whitehead will be glad to learn that such an organisation is in existence. It has for its object the preparation of the ground for the establishment of a professional institute for the education and registration of laboratory technicians not at present within the jurisdiction of the Institute of Medical Laboratory Technology, with which it will be in many ways comparable. During the interim period which must elapse before the institute can be fully established, an association, called for the time being the Science Technologists' Association, has been set up and has the temporary use of an office at 151, Victoria Street, London, S.W.1.

These two organisations—the I.M.L.T. and the S.T.A.—are independent of each other, although there is an abundance of common interest; and we are grateful to the I.M.L.T. for advice and practical assistance which have been freely given.

Membership of the new institute will be restricted to the holders of certain certificates and/or diplomas, the exact details of which have not yet been finally settled, although the general scheme has been agreed upon and pilot and preliminary courses of study are in operation at Paddington Technical College, London, W.9, and similar courses are contemplated elsewhere. The educational requirements are as follows:

Preliminary education should be at or approaching present school certificate or senior College of Preceptors certificate standard in selected subjects, such as elementary mathematics, English, and general science. In special cases, other evidence of general education would be considered.

The following technological courses are to be taken concurrently with general laboratory work in which the technician is normally engaged: (1) a 3-year course prior to a certificate examination; and (2) a course lasting a further 2 years prior to a diploma examination. Candidates who have satisfactorily completed the courses and passed the

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respective examinations will be awarded the certificate and diploma. Provisions have been made for older technicians who, though possessing wide and valuable experience, have reached a stage at which it would be unreasonable to insist upon the passing of a set examination.

In conclusion, may I draw attention to the fact that Dr. Whitehead implies that it is only among technicians in medical laboratories that a professional outlook exists? This is not in accordance with the facts. The science technician is no less conscious of the importance of his work and of the necessity of enduring without complaint many demands upon his time.

ROBERT J. FISHER
246, Pickhurst Rise, West Wickham, Kent. Vice-President, Science Technologists' Association.

LIVER EXTRACTS

SIR,—It is doubtful whether the maintenance dose of liver extract is always the same in any particular patient with pernicious anæmia, and for this reason the hæmatologist usually errs on the side of overdosage. With this reservation our experience supports Dr. McSorley's view that larger amounts of liver extract are required for maintenance therapy than is commonly realised, as the following analysis of a series of 65 patients attending our anæmia clinic will show:

Dose of liver extract (ml. per week)	*No. of cases*	*Mean Hb (g. per 100 ml.)*	*Mean corpuscular volume (c.μ)*
0·5	1	12·5	96
1·0	19	13·9	91
2·0	29	13·5	91
4·0	16	13·8	95

The aim which we have achieved is to keep the hæmoglobin and cell size within the normal range. The extract used was 'Anahæmin,' which we had ourselves tested, so that we knew that an injection of 2 ml. would produce a maximal rise of red cells over a period of two or sometimes three weeks in a patient in relapse. It seems a paradox that more liver may be required for maintenance than for the induction of a remission, and this seems to be one of the fields in which it is the *dernier pas qui coûte*.

SHEILA T. CALLENDER
Radcliffe Infirmary, Oxford. L. J. WITTS.

SIR,—It would be somewhat unfortunate if Dr. Wilkinson's recommendation in your issue of Feb. 5—that the intervals between doses of liver extract in the treatment of pernicious anæmia should not be greater than two weeks—should gain general acceptance.

Certain patients attending the clinic of this department have shown themselves able to maintain over years a satisfactory blood picture on 4 ml. of an active extract given at intervals of three months, a few more at intervals of two months, and the majority at intervals of from six to four weeks. In only relatively few cases does the maintenance of a satisfactory blood picture call for fortnightly doses, though it must be borne in mind that the requirement of patients under treatment may vary from time to time; relapse appears to occur even in the face of liver treatment and to demand temporarily an increase in dosage.

There is no danger of overdosage with parenteral liver extract, but it is wasteful and uncomfortable for the patient. Successful and economical treatment of pernicious anæmia demands observance of two points—the possession of a liver extract of known high potency, and periodical examination of the blood. The statement by Dr. Shaw in the same issue that no attempt has been made to assay quantitatively liver extract by clinical means ignores the work of Riddle,[1] Della Vida,[2] Emery and Hurran,[3] and many others. The whole question of the assay of liver extracts is discussed by myself, and the relevant formulæ given, in *Recent Advances in Clinical Pathology*.[4]

The dangers inherent in the presence upon the market of liver extracts either altogether inactive or of suboptimal potency have long been manifest and can only be met by the assay of every batch of liver before it is put into use. In this clinic use is made of no preparation which has not been subjected to such assay, in most cases in the clinic itself.

Dr. McSorley (Jan. 22) appears to fear that a red-cell count below the accepted normal is an invitation to the development of subacute combined degeneration of the cord. This is not the experience in this clinic. It is true that patients with nervous manifestations require in the initial stages of treatment intensive dosage of liver extract for long after the red cells have risen to a satisfactory level; but a stage is finally reached at which there is no further improvement in these symptoms and the dosage may then safely be reduced to a level sufficient to keep the red cells above about 4,500,000 per c.mm. In such cases it is advisable to use the cruder preparations and to shun those which have been subjected to much refinement with a view to concentration of the anti-anæmic factor.

Finally no case of pernicious anæmia can be satisfactorily treated without periodical examination of the blood. The practice of this clinic is to make such an examination every time the patient receives his injection and in no case at intervals of more than six months. With the facilities offered under the National Health Service such periodical examinations should everywhere be readily available.

The Royal Hospital, Wolverhampton. S. C. DYKE.

SIR,—The letters on this subject in your issue of Feb. 5 call for some comment. We can confirm Dr. Wilkinson's finding that the liver available for manufacture of extract varies in quality and is sometimes poor in anti-pernicious-anæmia factor. But we cannot accept Dr. Wilkinson's sweeping condemnation of the liver extracts on the market. We share Dr. Wilkinson's view that every batch should be tested clinically before release and we have invariably acted on this view, even when it involved pouring large batches of subpotent liver extract down the drain. It has even happened that, during a shortage of clinical cases, we had to withdraw our extract temporarily from the market, rather than issue inadequately tested material.

We cannot speak for other British manufacturers, but the official American practice is indeed what Dr. Wilkinson rightly deplores—namely, clinical tests on a single batch made by the proposed manufacturing process. The danger of the neglect to examine subsequent individual batches is confirmed by the values published by Rickes et al.[1] for the microbiological activity of some American commercial liver extracts. All were nominally 15 *U.S.P.* units per ml., but their "vitamin B_{12}" activities varied from 1·2 to 14 (mean 5·3) μg. per ml. Rickes and his associates consider 15 *U.S.P.* units to be equivalent to about 15 μg. of vitamin B_{12}.

At present we use the microbiological assay to supplement, though in no way to replace, the clinical test. Our practice is to standardise batches of liver extract microbiologically against the pure crystalline anti-pernicious-anæmia factor, and then to submit the extract to thorough clinical testing. So far the agreement between the two methods of assay has been good, considering the inaccuracy of clinical tests even on several patients. Thus we avoid wasting test cases on subpotent material, because this can be rejected on the microbiological assay alone. On the other hand, we are not prepared at present to rely solely on this test, particularly because of our finding (quoted by Mr. Shaw) that liver extracts contain four substances active in the microbiological assay, of which only two have been proved clinically active. The technique of paper-strip chromatography for the separation of these factors is being rapidly developed and we have little doubt that it will soon be put on a quantitative basis. It is hoped that clinical tests may eventually be replaced by this combination of chromatography and microbiological assay, but comparison of the two methods on a large number of batches can alone provide information to justify such a procedure.

Glaxo Laboratories Ltd., Greenford, Middlesex. E. LESTER SMITH
W. F. J. CUTHBERTSON.

1. Riddle, M. C. *Amer. J. med. Sci.* 1940, **200**, 145.
2. Della Vida, B. L. *Lancet*, 1942, ii, 275.
3. Emery, W. B., Hurran, W. J. *Brit. med. J.* 1945, i, 264.
4. Recent Advances in Clinical Pathology. London, 1947; p. 295.

1. Rickes, E. L., Brink, N. G., Koniuszy, F. R., Wood, T. R., Folkers, K. *Science*, 1948, **107**, 396.

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CEREBRAL ABSCESS IN AN INFANT

SIR,—Mr. Farley, in his interesting report last week, has surely missed the obvious diagnosis of the exciting cause.

Having adequately described a case of acute osteomyelitis of the upper jaw in an infant he goes on to say:

> "The abscess in this case probably arose from infection of the left cheek and thrombophlebitis of the facial veins . . . The left proptosis and orbital œdema suggest cavernous-sinus thrombosis. . . . There is now no clinical or radiographic evidence of maxillary infection."

It is quite unnecessary to postulate a cavernous-sinus thrombosis to account for the proptosis and orbital œdema, as these are not uncommon in acute osteomyelitis of the upper jaw. Recently, indeed, I saw such a case which presented with just these eye symptoms and no others. The question of an antrum infection, which was suspected, is not of much importance in these infants, as the infection does not arise in the nose or accessory sinuses but in the socket of the unerupted first molar tooth.

London, W.C.1. RICHARD CHIGNELL.

THE AIMS OF MEDICINE

SIR,—I have read Professor Adrian's address, published in your issue of Dec. 25, with considerable disappointment. His distinction commands great respect, and he was speaking to a large gathering of medical students. Yet it seems to me that he played the part of Mephistopheles. Life is to be under control, unapproved qualities will be drugged or dissected out, the mental will be subordinate to the physical. In the world ahead physicians will assume power and position. The paper seemed implicitly to deny that there are perhaps qualities and power of mind and spirit of which we dream not yet.

How will Professor Adrian fit his doctors for the power they are to wield? Can there be aims without a philosophy of medicine? In this world of which he dreams, who are to be the supermen who will select men to be doctors to inject the drugs and perhaps cut the nerve-fibres of a generation at birth? Will doctors be the obedient technicians of a ruling sect?

Professor Adrian admits that "there will always be successful psychotherapists whose effectiveness depends not on the particular theories they hold but on their general relation to their patients." Perhaps these men have in their souls (outmoded word) something lacking in many brilliant research-workers with their wonderful theories and knives. Many psychiatrists can dissect, but many seem not to have the qualities needed for integration. One recent development of these brilliant men "aims at the mind by deliberate interference with the structure of the brain." There is abundant evidence that the knife or electric current or drug can dull or diminish, but what evidence is there that these means of interference can create? The man who has had a leucotomy is no more a full man than is a eunuch. We can cripple and remove the consciousness of crippling, leaving a contented gelding or a steer. To what extent when we remove a part do we diminish a man? Because there is power of adaption, it does not mean the adaption is good.

"Power tends to corrupt . . . ." Is it true, and if true is it good, that "the doctors of the future will be in authority over mankind"? Will the doctors be comparably any wiser than their fellows than they are today? Perhaps as men become more mature there will be less need for experts, including doctors, and they will be more jealously watched and controlled by the community.

Professor Adrian speaks of doctors controlling the mind. We can only control or channel the human spirit in one direction if we open a new channel or enlarge an old one to give new forms of freedom. The force is there and must find expression. Can we create angels to aid us, for these doctors will need to be angels in intelligence above mortals! There is indeed need for care lest the men who work in laboratories get the power lust of Faustus or become genii of the bottle in the hands of ruthless men.

Whence comes this desire to control and what are the principles we seek? Is it to be expected that control from without will ever bring happiness like a penny-in-the-slot machine, or must it always be a by-product of living and dependent upon control from within?

If the doctor of Professor Adrian's world is not a true seer and a leader of vision, he will be a menace to be destroyed. Meanwhile one of the chief aims of medicine should surely be to develop men who are fitted to be "guide, philosopher and friend" as well as expert technician. There is need in university and hospital to assemble teachers who in addition to high degrees possess those other qualities and are inspired by a high philosophy of medicine.

Farnham Royal, Bucks. M. E. M. HERFORD.

INTRAVENOUS TREATMENT OF ANÆMIA WITH AN IRON-SUCROSE PREPARATION

SIR,—In view of the observations of Dr. Slack and Dr. Wilkinson in your issues of Jan. 1 and 22, we should like to draw attention to the work on saccharated iron oxide and allied iron compounds carried out in the department of pharmacology at Guy's Hospital in the last eighteen months.

The primary object of standardising a method of preparation of saccharated iron oxide has been achieved. Furthermore, by means of controlled methods it is now possible to produce samples of much smaller toxicity than those hitherto reported on in the literature. We should like to record our findings.

1. Saccharated iron oxide was prepared from the following analytical-grade reagents: ferric chloride hexahydrate, anhydrous sodium carbonate, sodium hydroxide, sucrose, and water. A systematic study of the reaction by which saccharated iron oxide is produced has been made, and the effect of each of the following points investigated independently: (*a*) the relative amount of each of the above substances entering into the reaction; (*b*) the sequence in which the above reagents are added; (*c*) the type of ferric hydroxide obtained; (*d*) the final carbonate content of the preparation; (*e*) the temperature at which the reaction is carried out; (*f*) the type of sugar added; (*g*) leaving or washing away the by-product—i.e., sodium chloride; (*h*) the final alkalinity of the preparation.

The first sample produced was made to correspond exactly to the original specimen of saccharated iron oxide reported on in THE LANCET [1] and was found to have the same toxicity in mice (L.D.50 = 180 mg. per kg.). Subsequently a method was found which made it possible to measure the effect of heat on saccharated iron oxide and thus to control the production of the various samples to a nicety. It was found that there was a linear relationship between toxicity and the effect of heating, as measured by the physical characteristics of the substance produced, thus making it possible to select the best samples of saccharated iron oxide for intravenous injection. The details of this method were described at the last meeting of the British Pharmacological Society. The best sample was found to have an L.D.50 of 300 mg. or 15 ml. per kg. of a 2% solution, as compared with the 180 mg. or 9 ml. per kg. of the original sample. A specimen of 'Ferrivenin,' when tested on mice by the same method, also gave an L.D.50 of 180 mg. or 9 ml. per kg.

2. This new preparation has repeatedly been given intravenously to several patients in doses of 300 mg. of elemental iron without the slightest toxic reaction. In this second series, altogether 7 patients have been treated without any toxic effects; 3 cases with hypochromic anæmia refractory to oral iron responded dramatically and maintained their new blood-levels for periods exceeding eight months. It is possible that even larger doses of this new preparation may be tolerated.

3. Compounds of iron with glucose or fructose instead of sucrose were found to form much more easily and require less heat for their preparation. In fact they can be prepared in the cold if left long enough. They also require much less of the sugar for the formation of the compound. They proved more toxic, however, with an L.D.50 of about 150 mg. or 7·5 ml. per kg. in mice.

1. Nissim, J. A. *Lancet*, 1947, ii, 49.

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They possess a strong anticoagulant action and animals injected with them show evidence of direct capillary damage, sometimes with pulmonary œdema and pleural effusion.

4. Samples prepared according to the method described by Slack and Wilkinson invariably precipitated on autoclaving. This is in agreement with the work on ferric glucosate and fructosate mentioned above. It is noticed that Slack and Wilkinson add sucrose to the ferric chloride over the water-bath at a temperature of 95°C and before neutralising. Solutions of ferric chloride are strongly acid (pH about 1·0) and readily split the sucrose to glucose and fructose. There is thus a variable amount of ferric glucosate in Slack and Wilkinson's preparation, depending on the degree of the splitting of the sucrose. Even when only a quarter to a half of the amount of sucrose is added as mentioned in their subsequent letter (Jan. 22), some of the sucrose still splits, as may be verified by means of Fehling's test. Indeed it is possible —and there is some evidence for this—that when the final addition of sucrose is made a double compound of iron is formed with glucose or fructose on the one hand and sucrose on the other. This is slightly more resistant to heat than the pure glucosate or fructosate, and can thus be autoclaved for 20 min. By that time the preparation appears to be changed again to the glucosate. The formation of these compounds explains the increased susceptibility of Slack and Wilkinson's preparation to heat and their finding that even an extra 5 min. in the autoclave causes precipitation. True saccharated iron oxide is much more resistant to heat and shows hardly any breakdown when autoclaved. The fact that Slack and Wilkinson found that infusions of 500 mg. produced mild intoxications and injections of 300 mg. frequent reactions—a fact stressed in your leading article of Jan. 1—also fits in with those observations.

A preparation made according to the directions given by Slack and Wilkinson in their letter and conforming to it in the final pH gave an L.D.50 of about 150 mg. iron or 7·5 ml. per kg., which is again about twice as toxic as our new preparation against which it was tested on the same batch of mice.

Lastly, we should like to point out that no serious effects have resulted from the intramuscular and subcutaneous injections of as much as 20 mg. iron as saccharated iron oxide, as previously reported.[1] Accidental injection outside a vein should never exceed 1 ml. since the very dark colour of the solution makes extravasation easily noticeable. Perhaps the greater alkalinity of ferrivenin (pH 11·4) and the high salt content of Slack and Wilkinson's preparation (sodium chloride not washed away) is responsible for the local effects described by them. The follow-up washing of the vein originally advocated has been dispensed with later on without any resulting thrombosis. The site of injection, however, is left free from pressure, and circulation through the vein is encouraged by movement of the arm after the injection.

JOSEPH A. NISSIM
Guy's Hospital, London, S.E.1. J. M. ROBSON.

BACK NUMBERS

SIR,—I wonder whether any of your subscribers who have preserved their copies of THE LANCET during the war years would be willing to part with them as a gift to the Max Planck Gesellschaft—an organisation of scientific research institutes now being formed in Göttingen with the active support of both British and German Authorities.

During a recent visit to Göttingen I realised that one of the greatest needs of these new institutes was for recent foreign scientific literature. This is now being met to some extent by supply of current issues of the most important journals; but the university libraries, as well as the newly formed Otto Hahn library, which serves the group of research institutes, are in serious need of the numbers of the war years to complete existing sets.

The Medical Research Institute is already in being under the energetic directorship of Prof. Karl Thomas, well known as the assistant and co-worker of Prof. Max Rubner in Berlin and later as director of the physiological institute of the University of Leipzig. A more complete file of THE LANCET is one of the important needs of his new institute. The volumes specially required are those between the second half of 1939 and 1945; but earlier volumes would also be welcome.

The war-time volumes are out of print. Any subscriber generously parting with them for the benefit of the institute would be not only helping to spread knowledge of the achievements of British medicine during the war years, but also making a gesture of international good will which would be very greatly appreciated.

HARRIETTE CHICK.
Lister Institute of Preventive Medicine,
Chelsea Bridge Road,
London, S.W.1.

EPSOM COLLEGE CENTENARY REGISTER

SIR,—I have undertaken the general editorship of this register, and I am finding great difficulty in tracing the parentage of many of the boys entering the college between 1855 and 1874. I ask readers who have knowledge of these early entrants to write to me. The smallest clue may be useful.

Cricklade, Wilts. T. R. THOMSON.

VEGANIN

SIR,—In your issue of Jan. 15 Professor Alstead asks for scientific evidence of the superiority of 'Veganin' over tab. codein. co. It would not be easy to provide such evidence, in view of the many difficulties met in testing analgesics. Nevertheless veganin tablets have an obvious advantage in that they disintegrate into a fine powder as soon as they are moistened, and as a result they are bound to be absorbed more easily than the "granite-like tablets" known as tab. codein. co. I was long ago convinced that veganin is in fact more efficient than other products said to be similar. After all, when different cooks put exactly the same ingredients into their cakes, the end-results are by no means always the same.

Edinburgh. M. C. MACQUEEN.

NURSING EXPERIENCE FOR MEDICAL STUDENTS

SIR,—Your preclinical correspondents, writing on their experience of nursing, are to be commended on their public spirit, but one cannot help feeling that their enthusiasm springs from novelty. However, the deplorable rift between the preclinical and clinical course is beside the point here. Undoubtedly their experience was of immense value; but so, for that matter, is a month's work in a coalmine. The question we must seriously ask ourselves is: "Could the time be better employed?" For the preclinical student, with his vacation of five months in the year, the answer is frankly "No." For the clinical student, overburdened as he is with one specialised appointment after another, no fixed holidays, and an enormous syllabus, the answer is surely "Yes."

The fact that students rarely perform a forceps delivery has already been mentioned. But this is perhaps the least important item from a formidable list of shortcomings. Only rarely does a student perform injections for piles or varicose veins, paracentesis, lumbar puncture, myringotomy, the lancing of a quinsy, or the setting of a fracture. How many newly qualified practitioners feel confident to administer a general anæsthetic without the encouraging presence of a proper anæsthetist? Indeed this list has almost no end. Yet all these are common procedures, which, if they have never been performed under supervision, can be fraught with the gravest consequences. On the other hand, a bedpan round, even if conducted with not quite the gracefulness of a State-registered nurse, is unlikely to endanger a patient's life.

Much emphasis has been laid on the comfort of the patient. Recent correspondence has shown how the patient's comfort is sacrificed in our hospitals. It is perhaps not generally realised that in hospitals the beds are made primarily for the sake of appearance. Often one is witness to a patient being waked because his bedclothes are disarranged. To train the student in these methods is to do more harm than good.

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There are many eminent physicians and surgeons at the London Hospital who, I feel sure, can make a bed no better than a student. But the student who acquires only a fraction of their wisdom will be of greater service to his patients than if he had the knowledge of ten ward sisters.

There seems to have been a remarkable loss of sense of proportion at the London Hospital. If the authorities really have a month to spare from the curriculum, which is incredible, they would confer far greater benefit on their students by making it a compulsory holiday. In this way they would at least be making a valuable contribution towards student health.

HERBERT BARRIE
Final year Student.

REGIONAL REPRESENTATION ON THE JOINT TUBERCULOSIS COUNCIL

SIR,—I have been instructed to reply to the letter of Dr. Sutherland and Dr. England in your issue of Jan. 22. Dr. Sutherland knows that the North Western Tuberculosis Society has not been well supported in the past by the Liverpool region; therefore its officers are from Manchester and areas remote from here who do not know our local problems. The representatives of the North Western Society on the J.T.C. report to the society, but the opinion of members is not sought before decisions are reached.

As the J.T.C. has asked to be represented on the Negotiating Committee, the other members of the committee will presume that this representative claims to speak for the doctors working in tuberculosis. When he is not representative of many of these workers, he has no right to make such a claim. The British Tuberculosis Association would have a better claim, but then again an inadequate one.

The J.T.C. has done good work in the past, but it is now trying to do work for which it is not suited; and if it is to do this new work it should be representative of regions and not of societies.

WILLIAM D. GRAY
Hon. Secretary, Liverpool Region Tuberculosis Society.
5, Brockholme Road, Mossley Hill, Liverpool 18.

Parliament

Too Many Patients

IN the House of Commons on Feb. 9 on the motion for the adjournment, Mr. MARTIN LINDSAY said that in Birmingham a large number of people had been arbitrarily instructed by the executive council to leave the doctors of their choice, whose patients they had often been for a large number of years. He could well understand that on the appointed day last year there was some confusion and that some doctors found that they were taking on more patients than they could deal with. For example, in his constituency of Solihull, a medical practitioner, Dr. Washington, discovered when things had been sorted out that he had over 3000 patients beyond the maximum figure of 4000 which had been laid down.

Obviously the executive council had to ask a number of these patients to find another doctor. But Mr. Lindsay questioned the method of selection of the patients who were to be removed from the doctor's list. The only fair method, he held, was to remove the more recent additions to the list. The one thing which the executive council should not have done was to give arbitrary instructions to people to leave a doctor when they had been his patients for a long time. Such treatment was a direct breach of faith in view of the repeated promises made by Ministers when the Act was passing through Parliament that there would be no interference with the personal relationship between doctors and patients.

Mr. Lindsay cited another Birmingham case, that of Dr. Lambie, who had 500 patients in excess of 4000 and had been told he must get rid of them unless he obtained an assistant by March 4. In spite of all his efforts Dr. Lambie had not been able to find an assistant because he was quite unable to offer accommodation for a married man and his family. Before July 5 last year this doctor had exactly the same number of patients as he had now and his practice was working no less smoothly now than it was then.

The limit of 4000, Mr. Lindsay considered, should not be a statutory maximum, but rather an approximate guide to the number of patients which a single doctor could treat. If a doctor was taking more patients than he could look after competently the patients had the remedy in their own hands. He begged the Minister to instruct executive councils that if the number of patients on a doctor's list was much too large they should in no circumstances remove arbitrarily from the list long-standing patients, but rather the more recent additions.

Sir PETER BENNETT, who also represents a Birmingham constituency, had received similar complaints. He had been asked to find how the selection was being made. It had been suggested to him: "It is a bit hard that doctors should be allowed to choose the good ones and get rid of those with whom they have to go to some trouble . . . doctors will take all the young and healthy ones . . . and unload from their panels, when they are overfull, the old ones who require a lot of attention." He did not suppose that that was really the method, but it was not surprising that people should say that sort of thing when they were parted from the doctor who had attended them for a long time.

Mr. ARTHUR BLENKINSOP, parliamentary secretary to the Ministry of Health, assured Mr. Lindsay that it was far from the intention of the Government or the executive councils that there should be any arbitrary decisions, and no such decisions had been taken. It had been understood that at the start there should be a broad latitude in regard to the agreed figure of 4000 patients on a doctor's list, because they were anxious that there should be no splitting up of families. But after discussion with the medical profession a circular was sent out from the Ministry to the executive councils last November suggesting that this matter should be looked at in view of the wide discrepancies which existed between the lists. He thought it was the general view of the medical profession, as well as of the Ministry, that it would be impossible to get the type of service which they wanted if some of the grossly overloaded lists were allowed to continue.

The Ministry suggested that the first action should be to try to prevent the addition of new patients to the lists, but it was understood that the executive councils should make decisions in accordance with the conditions in their areas. Before the Birmingham executive council were able to consider the matter Dr. Washington wrote to them saying that the number on his list was far too great and asking the council to help him to reduce it. He suggested that if he could limit his area to the district outside Birmingham where he had quite a large practice and where there were few other doctors to whom patients might go, he would be doing the right thing. In discussion with the council Dr. Washington indicated those he would wish to be removed from his list and the council notified the names after they had been agreed with the doctor concerned.

Mr. Blenkinsop thought this was a reasonable and fair thing for the council to do. It enabled the doctor to keep his practice going over the 4000 limit in an area where there were few alternative doctors to whom the patients could go, and he released patients for whom there were a number of other doctors available. It was probably true that it was difficult to get accommodation for married assistants. He did not know how difficult it was for single assistants. It might well be possible to get an assistant into Dr. Lambie's practice.

Many members of the medical profession, he added, felt that 4000 was too high a figure; and it was unfortunately true that there was a wide disparity between one doctor's list and another's. Therefore, it would be impossible to leave a doctor with well over 8000 patients on his list, whom, according to all medical experience, it would be impossible for him to deal with adequately, and for other experienced practitioners to have much smaller lists. It was essential for the benefit of the patients themselves that in the friendliest and most coöperative way possible they should get some redistribution between one extreme and the other.

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QUESTION TIME

What the Doctor Orders

Mr. E. H. KEELING asked the Minister of Health whether he was aware that some National Health Service doctors declined to write prescriptions for laxatives, first-aid dressings, antiseptics, and other household remedies which before the service came into existence were not normally obtained on a medical prescription; and whether he would make a statement on this matter.—Mr. A. BEVAN replied: It is the duty of a doctor under the National Health Service to prescribe any drug or prescribed appliance which he considers necessary for the treatment of a patient or for the prevention of disease, but it is no part of his responsibility to prescribe drugs and household remedies for healthy persons for purposes of self-medication.

Medical Superintendents and Hospital Committees

Mr. E. A. HARDY asked the Minister why medical superintendents were not allowed to attend hospital management committees in the Manchester regional area.—Mr. BEVAN replied: This is a matter for the committee concerned, but I have drawn attention to the desirability of making this arrangement.

Wigs under the N.H.S.

Major GUY LLOYD asked the Minister what sum had been expended and approved up to date on wigs supplied under the new health service.—Mr. BEVAN replied: Up to Feb. 5 the total approximate cost of those ordered was £36,500. Wigs are issued (in duplicate) through the hospital and specialist services if (*a*) the baldness is congenital or is due to an accident or some pathological condition; and (*b*) the wigs are considered necessary by a hospital specialist.

Splinter-proof Lenses

Mr. A. L. SYMONDS asked the Minister under what conditions he was able to supply unsplinterable spectacle lenses through the National Health Service.—Mr. BEVAN replied: Unsplinterable spectacle lenses can already be obtained through the hospital service where clinically necessary. I have decided to add them to the contributory range of spectacles under the supplementary ophthalmic services, but the terms on which they will be available are not yet settled.

Health Centres

Sir ERNEST GRAHAM-LITTLE asked the Minister what was his estimate of the number of health centres, and their cost, required to fulfil the functions assigned to them by section 21 of the National Health Service Act, 1946; and what was the earliest date at which he expected their provision, in view of the fact that the absence of them placed a burden upon those doctors who had joined the service under the expectation of health centres being supplied.—Mr. BEVAN replied: It is impracticable to make estimates. Work on the first new health centre will, I hope, start this spring.

Tropical Diseases Centre for London

Mr. IVOR THOMAS asked the Minister of Health what plans he had for the creation of a tropical diseases hospital in London worthy of the imperial responsibilities of the United Kingdom.—Mr. BEVAN replied: It is proposed to develop a tropical diseases centre as a unit of the University College Hospital group. The Colonial Secretary and I are most anxious to ensure that development shall be worthy of the object in view, and shall take place as rapidly as building and other difficulties permit.

Allocation of Petrol to Doctors

Mr. G. B. DRAYSON asked the Minister of Fuel and Power what instructions he had issued to his officers in connexion with the allocation of petrol to doctors by reason of the coming into force of the National Health scheme.—Mr. HUGH GAITSKELL replied: Regional petroleum officers have standing instructions to allow doctors sufficient petrol to meet their essential requirements. No special instructions were necessary, therefore, by reason of the coming into force of the National Health Service. Mr. DRAYSON: Is the Minister aware that there is an impression among some doctors that those doctors who have joined the National Health scheme are receiving more favourable treatment than those who have remained outside?—Mr. GAITSKELL: That impression is entirely without foundation.

Obituary

CUTHBERT HARRY ROGERSON

M.D. LOND., F.R.C.P.

Dr. C. H. Rogerson, who died in Baltimore on Feb. 10, at the age of 37, had already achieved much, and was marked for greater distinction.

Born at Wokingham, the only son of Mr. and Mrs. H. F. Rogerson, he was educated at Haileybury College. As a student at Guy's he was outstanding and won the Treasurer's gold medal for clinical medicine. He qualified in 1931 and graduated M.B. with honours in the following year. Through straitened circumstances he was unable to take the full course of resident appointments; but he became house-physician to the department for nervous diseases and was there attracted to psychiatry, finding in himself a natural gift for understanding human problems. Once having set his mind in this direction, he was determined to obtain the best possible education, and chose, like many others of his generation, to sit at the feet of Dr. Adolf Meyer. His ability was recognised by the award of a Rockefeller fellowship which enabled him to spend a year with Meyer at the Johns Hopkins Hospital in Baltimore. In 1935 he returned to Guy's and became Sir Alfred Fripp fellow with the object of making a special study of psychiatric problems in children. During the next few years he worked in close association with the late R. D. Gillespie, and he was largely responsible for creating an active and successful psychiatric unit for children, which attracted many postgraduate students and social workers.

The post of medical director of the Cassel Hospital at Penshurst then fell vacant, and Rogerson, not without some reluctance at leaving the academic field, was persuaded to apply. At this time his capacity as an administrator was unknown, and the Cassel Hospital needed a strong leader. The board were soon able to congratulate themselves on their choice, for Rogerson with his gentle ways and quiet persistence got what he wanted, and what he wanted was generally right. Thenceforward under his management the Cassel throve despite war difficulties and dislodgment. During these years he carried a heavy personal load. Short of staff, in new quarters, and living with his small family under conditions of considerable hardship, he kept the tradition and spirit of the hospital alive and growing towards the time when it might be re-established in its old home.

When the war was over Rogerson was invited to become director of the Seton Institute at Baltimore. It did not take him long to make up his mind to accept this offer. Although he had enjoyed his life and work at the Cassel, his interest was in the whole field of psychiatry and he felt he had had long enough with children and the neuroses. He had also gained confidence in his administrative powers, and he looked forward to the task of reorganising a large and somewhat old-fashioned mental hospital on modern lines. Before he fell ill about a year ago he had seen his plans develop in a way which made him happy. He had collected a staff of keen young men, established a satisfactory liaison with the Johns Hopkins, and organised postgraduate teaching rounds of a high standard. A colleague who attended one of these two years ago writes: "I carried away a vivid memory of the enthusiastic regard for their chief shown by the staff. Rogerson deserved this. He looked, and perhaps was, a shy person, but beneath his unassuming manner there was great charm and a steady enthusiasm for his work which was infectious. He had also a real sense of humour which prevented him from becoming intolerant of himself and others in difficult times. One hoped that when he had completed his task in the United States he would have returned to a senior post in this country."

Rogerson did not write many papers. In his early days this may have been due to diffidence. He was certainly not a person who would rush into print to establish a reputation for himself, and in later years he was too busy with the joint cares of clinical work and administration. He was elected F.R.C.P. in 1945.

He married in 1936 Bettie, daughter of Dr. Allen W. Freeman, formerly dean of Johns Hopkins School of Hygiene and Public Health, who survives him with two sons.

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ROBERT CRANSTON LOW

M.D. EDIN., F.R.C.P.E.

THE death is announced of Dr. Cranston Low, consulting physician to the skin department of Edinburgh Royal Infirmary. Born on New Year's day 70 years ago, he had a distinguished career at Merchiston Castle School and at Edinburgh University, where he graduated M.B. in 1902. Two years later, after holding house-appointments at Edinburgh hospitals, he took his M.R.C.P.E. and was appointed clinical assistant in the skin department of the Royal Infirmary.

In 1906, after a year spent on the Continent under such men as Neisser of Breslau and Unna of Hamburg, he returned to Edinburgh to become assistant physician to the skin department. In the same year he was elected F.R.C.P.E. He was awarded a gold medal for his M.D. thesis in 1924 when he was also appointed physician to the skin department and lecturer in dermatology to the university. With Miss Anne Rae, he created a large number of wax casts which rivalled the best collections on the Continent, and his stimulating lectures and clinics will be recalled by many of his old students.

Never robust, he retired because of ill health in 1933, though he took an active part as consulting physician in the building of a new department of dermatology and was chosen president of the British Association of Dermatology in 1937. When war came in 1939 his sense of duty brought him out of retirement to a post as lecturer in the bacteriological department of the university. Here he proved his versatility by mastering another branch of his profession, and in 1947, with Mr. T. C. Dodds, F.I.M.L.T., he produced an *Atlas of Bacteriology* which had an immediate success. At the time of his death he was superintendent of the laboratory of the Royal College of Physicians of Edinburgh, which he had also served as a member of council.

As well as many articles on dermatological subjects, Cranston Low wrote several monographs, such as *Carbon Dioxide Snow* and the classic *Anaphylaxis and Sensitisation*. The fourth edition of his *Common Diseases of the Skin* will be published in the near future. For the illustration of these books his talents as an artist were invaluable, but this gift was revealed more fully in his delightful water-colours. G.A.G.P., to whom we owe much of this memoir, writes of his old teacher and friend: "Although not of a gregarious temperament, Cranston Low had a host of friends of all ranks and ages. These knew him as a high-principled sensitive gentleman, with a hatred of shams and hypocrites, and with a charming individual sense of humour and a keen zest in life. His name is known to dermatologists all over the world, and by them he will be sadly missed not only for his outstanding work in his specialty but also for his attributes as a loyal colleague."

Dr. Cranston Low was twice married. His second wife, formerly Miss Alice Grant, survives him with their son, Dr. Norman Low.

ROBERT LESLIE DODDS

M.CH. BELF., F.R.C.S., F.R.C.O.G.

Mr. R. L. Dodds, who died on Jan. 26 at the age of 50, was born in Dundee, the son of the Rev. R. W. Dodds. He was educated at Belfast at the Methodist College, and his medical course at Queen's University was interrupted during the 1914-18 war by service as a surgeon sub-lieutenant in destroyers. On his return to Belfast he graduated with honours in 1920, and after holding a house-appointment at Swansea General Hospital he became an anatomy demonstrator at his own university. Later he came to London as obstetrical registrar at Charing Cross Hospital. In 1927 he took his F.R.C.S. and in the same year obtained his M.CH., with commendation. Appointment to the staffs of the City of London Maternity Hospital, the Samaritan Hospital, the French Hospital, and the Bearsted Hospital followed, and among his gynæcological colleagues he quickly established his reputation as a sound surgeon, an excellent diagnostician, and a fine lecturer. In 1934 he took part in the reorganisation of the London County Council maternity services, and he continued to be associated with this work as consultant at St. James' Hospital. During the late war he served as a major in the R.A.M.C. till ill health forced him to give up his commission in 1944.

A. D. writes: "Leslie Dodds combined personal charm and professional efficiency. His natural good looks were enhanced by a singular grace of manner. His unfailing courtesy, through no conscious effort of his own, made him immensely popular with acquaintances and patients alike, while to those who had his closer friendship his company was invariably interesting and pleasurable.

"In his work Dodds was an expert of the best type. In the various hospitals to which he was consultant he had under his care a large number of beds, and the experience so gained made his obstetric opinion one of the best in London. He was a dexterous operator, and many a young gynæcologist owes much to the advice and tuition he was always ready to impart. Yet he was modest to a degree, and his self-effacement prevented his qualities being more widely appreciated. His personal courage served him in good stead during two wars, in both of which he saw active and dangerous service, and his unswerving loyalty was rewarded by the warmth with which his friendship was returned. His premature death was a heavy blow, for his type is becoming increasingly rare in this competitive world; but the memory of his kindly, humorous smile will remain long in the thoughts of his friends."

Appointments

ANGUS, G. A. W., M.B.Edin., D.P.M.: psychiatrist to mental health service, Ayr.
GALSTAUN, S. G., M.A. Camb., M.R.C.S., D.M.R.E., F.F.R.: asst. radiologist, Prince of Wales Hospital, Plymouth.
MIDDLEMISS, J. H., M.D. Durh., D.M.R.D., F.F.R.: director, radio-diagnostic department, United Bristol Hospitals.
WEST, PETER, B.M. Oxfd, M.B. Lond.: house-surgeon, Hospital for Sick Children, Great Ormond Street, London.

Births, Marriages, and Deaths

BIRTHS

ALMOND.—On Feb. 8, at Burghclere, near Newbury, the wife of Dr. John M. Almond—a daughter.
BENNETT.—On Feb. 9, in London, the wife of Dr. Reginald Bennett—a daughter.
BIELENKY.—On Feb. 12, in London, the wife of Dr. David Bielenky—a daughter.
BUCKELL.—On Feb. 4, at Poole, the wife of Dr. E. W. C. Buckell—a son and a daughter.
BUXTON.—On Feb. 10, at Surat, India, the wife of Dr. N. A. Buxton—a son.
CROSBIE.—On Feb. 8, at Stanmore, the wife of Dr. Desmond Crosbie—a daughter.
GUILD.—On Feb. 9, at Simonstown, the wife of Surgeon Commander W. J. Forbes Guild, R.N.—a son.
HOOKER.—On Feb. 7, at Ludlow, the wife of Dr. A. G. Hooker—a son.
JAMES.—On Feb. 9, at Horsham, the wife of Dr. Trevor James—a daughter.
RICE.—On Feb. 6, at Worthing, the wife of Dr. David Rice—a daughter.
RORIE.—On Feb. 10, the wife of Dr. R. A. B. Rorie—a daughter.
SHARPLEY.—On Feb. 9, the wife of Dr. John Sharpley—a son.
WEST.—On Feb. 7, in Edinburgh, the wife of Dr. Ranyard West—a son.
WILKINSON.—On Feb. 3, at Stocksbridge, near Sheffield, the wife of Dr. P. J. Wilkinson—a daughter.

MARRIAGES

DEANE—WALKER.—On Feb. 5, at Great Yarmouth, K. R. Hamilton Deane, M.R.C.S., to Valerie Walker (née Nightingale).
LEDGARD—FELL.—On Feb. 11, at Port Said, Egypt, Herbert Arthur Ledgard, M.B., to Marjorie Eugenie Fell.
LILLIE—HUTCHISON.—On Feb. 5, at Beverley, Douglas Lillie, M.B., to Elisabeth Hutchison.
WALLACE-JONES—BOSTON.—On Feb. 5, at Liverpool, Dudley R. Wallace-Jones, surgeon lieutenant, R.N.V.R., to Jacqueline Boston.

DEATHS

DAVIES.—On Feb. 10, at Plymouth, Arthur Llewellyn Davies, M.A. Oxfd, M.R.C.S.
HALSTEAD.—On Feb. 1, at Bideford, George Ezra Halstead, B.A., M.D., B.SC. Lond., aged 87.
HARNETT.—On Feb. 9, at Hadley, Barnet, William George Harnett, J.P., M.A., M.D. Dubl., aged 68.
JERRAM.—On Jan. 21, in Rhodesia, Ursula Jerram, M.R.C.S., D.C.H.
LYS.—On Feb. 6, at Bere Regis, George Lys, M.R.C.S., aged 81.
MCNEILL.—On Feb. 7, at Tettenhall, Wolverhampton, Ina Lochhead McNeill, M.B. Glasg., aged 79.
MARSH.—On Feb. 6, at Llanfrechfa, Newport, Mon., Octavius de Burgh Marsh, O.B.E., B.A., M.B. Camb.
ROGERSON.—On Feb. 10, in Baltimore, Cuthbert Harry Rogerson, M.D. Lond., F.R.C.P., D.P.M.

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Notes and News

HUNTERIAN FESTIVAL DINNER

PRESIDING at the Hunterian dinner of the Royal College of Surgeons on Feb. 14, Lord Webb-Johnson read a message from THE KING expressing His Majesty's interest in plans for the restoration of the college.

THE PRINCESS ROYAL, who attended the dinner with the Duke of Gloucester, said that this was the first occasion on which women had been present: their numbers were not large, but they were grateful.

Mr. J. A. BEASLEY (High Commissioner for Australia) spoke of the success of the Sims travelling professorship, and the recognition of the Australian primary fellowship. Post-graduate students from Australia were deeply impressed by the college and its welcome, which would be enhanced by opportunities of residence in the new Nuffield College. The welcome had more than a professional significance; the visitors came to learn more than surgery. "We must all," said Mr. Beasley, "carry a responsibility a little beyond our own interests." Lord WEBB-JOHNSON pointed out that though the college was constantly welcoming men from abroad, the traffic was not one-way: it kept in touch with every country where medicine was taught in English. It had a great tradition in teaching; and after the war the need for a large development had become obvious. Big endowments had been received from Sir William Collins, and the college had had steady encouragement from the Minister of Health. To provide education on the present scale was nevertheless a serious strain on resources, and the college sought close partnership with the University of London. It would concentrate on the scientific side of surgery, as custodian of the Hunter tradition not only for British medicine but for the world.

Mr. NORMAN ROBERTSON (High Commissioner for Canada), responding to the toast of The Guests proposed by Mr. L. E. C. Norbury (vice-president), said that the Dominions appreciated the great effort made by the college in these difficult years. Prof. LILIAN PENSON (vice-chancellor of the University of London), also responding, spoke of London as richer than any other city in the world for scholarship, research, and the maintenance of a high tradition in learning.

Mr. ZACHARY COPE (vice-president) proposed the health of the Hunterian orator in verses praising his virtues and versatility. Mr. HENRY SOUTTAR, in his reply, expressed his belief that some day the Physicians would join with the Surgeons in creating an academic medical centre for the British Commonwealth. When he was a student the college resembled a mausoleum, but now at any time 300–400 students could be found there hard at work. Continuing the theme of his Hunterian lecture, he urged that it should be a place where the surgeons of the future would follow George Robey's injunction to Stop, Look, and Listen.

HOME HELPS

AT a meeting of the National Association of Home Help Organisers, held in London on Jan. 22, Sir Wilson Jameson rightly described this service as one of the most important and integral parts of the National Health Service. If domestic help, as well as nursing and medical attention, could be given effectively in the home, many patients, he said, could be kept out of hospital who would otherwise go in, and many others could be discharged from hospital earlier than is customary. He commended the scheme of training now being started by the National Institute of Houseworkers, and suggested that home helps should be encouraged to appreciate the value of the service they are giving; some badge or mark of distinction might be introduced for those who had given long service. It seems that a successful Home Helps' Club has already been started at Hackney.

A few difficulties about the cost of the service have been encountered, some householders finding the assessment scale high. Sir Allen Daley said that the London County Council is applying the fractional system for the present—the patient paying for the number of hours given. Organisers find this the fairest method: when patients are charged for the time given it is possible to allocate several cases to the same home help; whereas if a flat-rate is charged the patient who is ill for a long time suffers hardship.

In some parts of London home helps have volunteered for night service; and one organiser mentioned that home helps in her area are paid 2*s*. a night in addition to the weekly wage. It was suggested that where tuberculous patients need help, only women over the age of 40 should be sent. Safeguarding precautions are already issued by medical officers of health for the instruction of home helps and patients. If a relative has to give up paid work to look after a tuberculous patient she becomes eligible, in most areas, to be paid as a home help.

University of Cambridge

On Feb. 5 the following degrees were conferred:

M.A.—John Marks.
M.D.—J. A. Glover.
M.B., B.Chir.—R. B. McGrigor,* J. W. MacLeod,* F. D. Schofield,* P. J. Andrew,* J. G. Gill,* Jeffrey Halford,* J. C. Burne,* Margaret L. Cox.*

* By proxy.

University of London

Dr. G. L. Brown has been appointed to the Jodrell chair of physiology at University College from Oct. 1.

Dr. Brown, who is 46 years of age, was educated at the Botcler Grammar School, Warrington, and the University of Manchester, where in 1924 he took his B.SC. with honours in physiology and was awarded a Platt physiological scholarship. The following year he took his M.SC. In 1928 he graduated M.B., being awarded the Bradley surgical prize and the medal in operative surgery, and in the same year he was appointed lecturer in physiology at the University of Leeds. He worked there on gastric innervation with the late B. A. McSwiney and on transmission through sympathetic ganglia. In 1934 he joined the scientific staff of the Medical Research Council, working in Sir Henry Dale's laboratory on transmission at nerve-endings by acetylcholine. In the early years of the war he worked on military problems, spending some time in the laboratory at Lulworth, where he took part in the development of the all-round-vision tank cupola. In 1942, when the Royal Naval Personnel Research Committee was set up, he became its secretary, and until 1945 he was directing work in his own laboratory on underwater physiology, dealing particularly with problems affecting submarine crews and divers using self-contained gear. He and his colleagues have now returned to their former interests and are studying ganglionic and neuro-muscular transmission. Since 1941 Dr. Brown has been secretary of the Physiological Society. He was elected F.R.S. in 1946 and appointed C.B.E. in 1947.

The title of professor of neuropathology in the university has been conferred on Dr. Alfred Meyer in respect of the post held by him at the Institute of Psychiatry.

Royal College of Surgeons of England

At a meeting of the council held on Feb. 10, with Lord Webb-Johnson, the president, in the chair, the appointment of Mr. V. Zachary Cope as Bradshaw lecturer was announced. Mr. Julian Taylor was re-elected and Mr. T. A. Hindmarsh, Mr. R. J. McNeill Love, and Mr. Digby Chamberlain were elected members of the court of examiners.

Mr. J. S. Arkle and Mr. F. C. Hunt were elected to the fellowship of the college ad eundem. The Hallett prize was awarded to I. S. R. Sinclair.

A diploma of membership was granted to C. P. Cotterill; diplomas were also granted to those named in the report of the comitia of the Royal College of Physicians (*Lancet*, Feb. 5, p. 347).

Royal College of Physicians of Ireland

At a meeting of the college held on Feb. 4, the following were admitted to the membership: T. D. Hanratty, R. W. M. Strain, F. G. C. Walker.

British Postgraduate Medical Federation

Postgraduate travelling fellowships for 1949–50, tenable for one year, have been awarded to J. V. Crawford, F.R.C.S., of the London Hospital (neurosurgery, U.S.A.); J. S. Prichard, M.R.C.P., of the National Hospital, Queen Square, and the Postgraduate Medical School, Hammersmith (neurology, U.S.A. and Canada); R. D. Tonkin, M.R.C.P., of Westminster Hospital (general medicine, U.S.A. and Canada); and J. E. M. Whitehead, M.B., of St. Thomas's Hospital (bacteriology, Scandinavia).

Lebanon Hospital for Mental Diseases

A colour film of this hospital, which is at Asfuriyeh, near Beirut, will be shown at Manson House, 26, Portland Place, London, W.1, on Tuesday, March 1, at 8 P.M. Lord Moran, P.R.C.P., will preside, and the film will be introduced by the Minister for Lebanon and the Minister for Transjordan. There will be a second showing on the following night, at 7 P.M., when the chairman will be Dr. J. C. Sawle Thomas, and the speakers will be the Minister for Syria and Miss Lettice Jowitt. Tickets may be had from the Lebanon Hospital office, Drayton House, Gordon Street, W.C.1.

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Royal College of Obstetricians and Gynæcologists

At a meeting of the council held on Jan. 29, 1949, with Sir William Gilliatt, the president, in the chair, Sir Henry Dale, O.M., F.R.S., and Prof. J. Heyman, of Stockholm, were elected to the honorary fellowship.

The following were elected to the membership:

G. McG. Barr, A. C. Barthels, D. W. Bentinck, Bimala Bhattacharya, D. K. Black, Kathleen M. Bower, G. C. Brentnall, Muriel Brighton, C. H. Brown, D. P. Cocks, H. J. A. Conte-Mendoza, Edward Cope, F. A. L. da Cunha, F. B. Davidson, Jyotsna Dei, Frank Denny, Nagala Subhadra Devi, C. J. Dewhurst, Kathleen A. D. Drury, J. G. Dumoulin, J. M. Duncan, Lamia Taha El-Badri, B. H. Ellis, H. R. England, I. B. Faris, B. J. Frankenberg, J. S. Fraser, W. K. Frewen, G. B. Gibson, L. S. Glass, Cecilie Greig, E. I. Holloway, C. G. Irwin, W. H. Laird, R. G. Law, L. E. Lotimer, R. L. Lunt, J. C. McCarroll, J. A. McGhie, J. F. McInerney, R. M. McIntosh, I. D. Macintyre, A. A. McKirdy, A. T. McNeil, J. H. Maloney, S. M. Medine, Gardiner Mitchell, J. E. E. Morgan, N. F. Morris, Chunilal Mukherjee, Naizby Noble, E. I. Ostry A. F. Pearson, H. E. Pellew, D. A. Ranasinghe, B. C. M. Reed, W. A. Robson, E. S. Rogers, J. K. Russell, C. R. Sluming, D. F. Smith, Zubaida Haji Yousof Sobani, D. B. Stewart, Arcot Sundarama Subramani, Jack Suchet, Eleanor Tennant, Mary E. Tighe, Mary U. Wilkin, E. O. Williams, E. G. Zacks.

From Australia the following were also elected to the membership:

J. M. Buchanan, S. E. Craig, H. G. Furnell, L. W. Gall, G. T. H. Harris, J. A. Love, H. A. McCredie, H. K. Porter, J. S. Reid, R. B. O. Stevenson, B. M. Sutherland.

The following from New Zealand were awarded the diploma in obstetrics:

Kelson Brasted, A. L. Bryant, F. L. Clarke, E. N. S. D'Arcy, E. M. Elder, R. C. Gordon, G. H. Green, R. H. Trevor Holmden, Barry Kahlenberg, M. D. Matich, F. A. H. Neate, K. L. Park, Irene G. Rhodes, H. A. A. Stevely, W. H. C. Teppett.

Medical Society of London

Dr. Horace Evans will deliver the Lettsomian lectures on Mondays, Feb. 28 and March 7, at 9 P.M., at the house of the society, 11, Chandos Street, W.1. He is to speak on Richard Bright, Before and After.

Contracts of Hospital Medical Staff

It has now been officially announced that hospital medical and dental staff holding provisional contracts under the National Health Service expiring on March 31 are to have these extended until July 4.

Course on Rheumatic Diseases

Prof. Bruce Perry will give the inaugural lecture in a course to be held at the rheumatism unit, St. Stephen's Hospital, Fulham Road, London, S.W.10, on Saturday and Sunday, March 26 and 27. Other lecturers will include Dr. Francis Bach, Dr. Grace Batten, Dr. Philip Ellman, Mr. A. G. Timbrell Fisher, Dr. Blake Pritchard, Dr. David Shaw, Dr. A. G. Signy, and Dr. Margaret Snelling.

Hunterian Society

Speaking at the annual dinner in London on Feb. 10, Sir Walter Monckton, K.C., recalled that John Hunter was by common repute the worst witness that ever appeared in a court of law. Dr. G. R. Mather Cordiner, the president, said that the society, though old, was certainly not senile; a large number of young men were joining its ranks. Speaking of present trends in medicine, he asked whether the haste to improve might not carry with it the danger of impairing freedom and thus discouraging men with an adventurous spirit—such as Hunter had been—from joining the profession. Dr. Franklin Bicknell suggested that men had shown little adaptability to the difficult circumstances of present-day life. Wives, on the other hand, had performed "evolution for two." As a possible patient, the Lord Mayor of London was alarmed by the president's suggestion that adventurous spirits should be encouraged to enter medicine. He went on to emphasise the value of free exchange of medical men between the countries of the Commonwealth. Mr. A. Dickson Wright repeated his earlier jeremiad on the topic of "weeping and wailing and nationalisation of teeth." Dealing with The Guests, who included the chairman of the Merit Awards Committee, he remarked that whereas the Israelites had once turned to the hills, "we must now turn our eyes to the mountains of Moran where they sweep down to the sea of our discontent. I hope this will help me when my turn comes. Perhaps it won't." Sir Roland Burrows, K.C., and Sir Henry Dale, O.M., responded to his toast. The Hunterian gold medal for 1948 was presented to Dr. Jack Lieber.

British Council

Dr. Margaret Suttill, who has been on the staff of the council since 1945, has been appointed director of the medical department in succession to Dr. G. A. W. Angus.

Royal Appointments

Rear-Admiral K. A. I. MacKenzie has been appointed honorary physician to the King in place of Surgeon Rear-Admiral Sir Henry White who has retired, and Surgeon Captain C. N. Ratcliffe honorary physician in place of Surgeon Vice-Admiral Sir Henry Colson who has retired.

Electrophoretic Analysis

The physical methods group of the Society of Public Analysts and Other Analytical Chemists is holding a discussion on this topic at the University, Nottingham, at 3.30 P.M. on Friday, April 1. Doctors are invited to attend.

Society for the Study of Addiction

Dr. Pablo Wolff, of Buenos Aires, will deliver the second Kelynack lecture at 1, Wimpole Street, London, W.1, on Thursday, March 3, at 5 P.M. He is to speak on Problems of Drug Addiction in South America.

Supplies of X-ray Film

The quantity of X-ray film distributed for use in this country was 20% greater in 1948 than in 1947; and it is hoped that supplies will be at least 25% greater this year than last. The Ministry of Health has informed hospital authorities that this additional provision may not suffice to bridge the gap between demand and supply; and the most stringent economy is asked.

Lieut.-Colonel G. H. C. Ovens, professor of clinical surgery in the University of Alexandria, has been appointed O.B.E. for services in Palestine. From 1946 to 1948 he was adviser in surgery to the Palestine command.

CORRIGENDUM.—The qualification of Mr. H. S. Grainger, who last week wrote a letter on The Wrong Drug, should have been given as PH.C.

Diary of the Week

FEB. 20 TO 26

Monday, 21st

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Mr. D. F. Ellison Nash: Development of Micturition Control. (Hunterian lecture.)

Tuesday, 22nd

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: Histopathology of the Skin.

Wednesday, 23rd

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. W. S. Lewin: Acute Subdural and Extradural Hæmatoma in Closed Head Injuries. (Hunterian lecture.)
INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, S.E.5
2.45 P.M. Prof. W. E. Le Gros Clark, F.R.S.: Organisation of the Cerebral Cortex.
HARVEIAN SOCIETY OF LONDON
8.15 P.M. (26, Portland Place, W.1.) Dr. A. J. Amor: Industrial Medicine.

Thursday, 24th

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. Robert Roaf: Treatment of Residual Disability following Injuries of the Peripheral Nerves of the Upper Extremity. (Hunterian lecture.)
UNIVERSITY OF LONDON
5 P.M. (Westminster Medical School, Horseferry Road, S.W.1.) Prof. B. G. Maegraith: Malaria as a World Problem.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, S.W.1
4.30 P.M. Neurology lecture-demonstration.
MEDICO-LEGAL SOCIETY
8.15 P.M. (26, Portland Place, W.1.) Mr. Wilfred Button: Pensions Appeals Tribunals.
HONYMAN GILLESPIE LECTURE
5 P.M. (Edinburgh Royal Infirmary.) Dr. A. Whitley Branwood: Clubbing of the Fingers.

Friday, 25th

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, W.1
8 P.M. Dr. Robert Sutherland: Individual and Social Factors in Venereal Disease.
LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Mr. D. S. M. Barlow: Treatment of Empyema.
SCOTTISH SOCIETY OF THE HISTORY OF MEDICINE
5.30 P.M. (9, Queen Street, Edinburgh.) Dr. H. P. Tait: History of Pædiatrics in Scotland.

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PHYSIOLOGY, SCIENCE, AND MEDICINE*

W. H. NEWTON
M.D., M.Sc. Manc., D.Sc. Lond.
PROFESSOR OF PHYSIOLOGY IN THE UNIVERSITY OF EDINBURGH

THE evolution of physiology is epitomised in the history of the Edinburgh chair, covering a period of 224 years. Its holders, if not always individually typical of their precise period, faithfully mirror in sequence the changing significance of the subject. Even the name has changed from the institutes of medicine, meaning the principles on which medicine is based, to physiology, which is now defined as "the branch of biology dealing with the processes, activities, and phenomena incidental to and characteristic of living organisms." A man may devote his whole life to it and give no more than a passing thought to the influence of his researches upon medicine. No longer a branch of medicine in the ordinary sense of the words, it is like a child which has grown up, made other connexions, and raised a family of its own. Biochemistry is already independent, and biphysics is being weaned, while a precarious independence is enjoyed by less defensible offshoots, such as nutrition, endocrinology, and neurophysiology. The process is, however, common to all branches of knowledge. They grow, they divide. They assume names which serve a purpose, but which nobody regards as representing particularly fundamental divisions.

The special point of interest, so far as physiology is concerned, is that the parent, medicine, still enjoys robust health, shows no signs of incipient dissolution, and expects a certain tribute of filial duty. No-one, on the contrary, is likely to suggest to exponents of the fundamental sciences that their students will not be good natural philosophers if they are taught too much about electronics and too little about oils, though this may conceivably be true. Natural philosophy, in its general sense, has become an ancestor. Parental survival implies no real discord between the medical and scientific aspects of physiology, as I hope to show, but a false contrast has sometimes been made between them, because medicine and science in the abstract can assume the quality of ideologies. The emotional loyalty which each can command has occasionally been recruited to causes in which they were not truly the contending parties.

MEDICAL CURRICULUM

A battle-ground often chosen for this supposed rivalry has been the curriculum of the medical student, and the question has been how far he shall be made acquainted with the uncertainties and problems of physiology, and how far these should be ignored in the interests of giving him, as rapidly as possible, a working knowledge of the human body which will serve as an introduction to his serious study of medicine. I do not wish to dwell too long on this largely sterile controversy, the extremists on either side of which can scarcely expect to be taken seriously. Their arguments are well known, and I do not propose to repeat them. At the expense of another brief digression, however, I feel it is worth while drawing attention to the real difficulties of the teacher, which have very little to do with the alleged antithesis.

Task of the Student

The student comes to his first lecture on physiology with an ignorance of the human body which those of us who are familiar with it cannot easily imagine. In eighteen months he has to master a language in terms of which he will think for the rest of his life. It must be remembered that for the medical student this includes not merely a superficial knowledge of the position and relation of organs sufficient for understanding physiology but also the details of human anatomy. In my day there were still surgeons—there may have been physicians too—who would welcome the newcomer to the wards with the robust assurance that he was now starting on the real thing, and should put behind him such milk-and-water pastimes as physiology. That attitude has been replaced by something a little more critical, but there is a paradoxical sense in which the advice is well worth pondering. I like to think it is the sense in which it was meant. By the time he enters the hospital the ideal student should be so familiar with the anatomy and physiology of the human body that he can read the consequences of an infection here or a degeneration there as readily as he grasps the meaning of a paragraph in a book written in his native language. He should not need to think consciously whether the respiration, the circulation, or the digestion is affected, or how the impairment of one can embarrass the others, any more than the reader recalls the meanings of individual words or dissects a paragraph sentence by sentence. The whole picture should present itself to his mind simultaneously. This would be a very ideal student, but the degree to which the ideal is attained is a measure of the confidence with which a man can concentrate on the rungs of the ladder which lie ahead of him.

This transformation of the student from one who physiologically cannot spell, who has never seen or imagined living tissues in action, into one to whom the functions of individual tissues and organs are commonplace and who can understand how they are all interrelated in the wonderful equilibrium of the healthy organism, is the fundamental event in the education of a doctor, or, for that matter, of a scientific physiologist. He must perforce acquire the knowledge piecemeal, he must be intellectually satisfied of its validity, and then he must think about it and synthesise it until he understands how the body works as a whole. Once that has happened, every subsequent piece of knowledge he acquires, at whatever stage of his career, slips into its proper perspective, and he is in a position to acquire experience, either medical or scientific.

Task of the Teacher

The task of the teacher is to help the student through this metamorphosis. The student cannot learn everything, and within the narrow limits of the time available, on the one hand, and what it is essential for him to know, on the other, a selection of facts and topics is necessary. I do not think the details of the selection matter very much, so long as the final integration is achieved—the revelation, as it were, accomplished. I regard it as sensible not to use a frog for a demonstration when a man will do just as well, and I believe that a deranged physiological mechanism as seen in a patient may throw a flood of light on the normal, However, should a student embark on his clinical career with an imperfect equipment of fundamental knowledge, the least likely thing to have been wrong is the factual content of his teaching. There are books full of facts which he is supposed to read. Nothing could be more fallacious than the notion that what a student knows is what his teachers have taught him. *How* they have taught him may have some influence, and so may his willingness to learn. Interest begets industry, industry begets knowledge, and knowledge begets understanding. In no subject is understanding more important than in physiology.

Length of the Course

The most important factor next to the relationship between teacher and student and the attitude of the latter towards his work is that of time. The nine months which have hitherto been allotted to the study of physiology for medicine in this university is hardly sufficient for the mental development I have outlined to be other than precocious. The eighteen months

* Inaugural lecture abbreviated.

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which will be available in the future should allow it to take place at a more normal rate and to be very much more solidly founded.

The question is not, therefore, whether the instruction in physiology should be vocational or scientific during this early period, for at this stage the two are not mutually exclusive. The question is whether a certain kind of foundation can be laid. I implore the student to whom the practice of medicine is the be-all and end-all to abandon the seductive idea that he can from the outset pick and choose what will be useful in the future and reject the remainder of what is presented to him. In that way, instead of building an edifice capable of being furnished, he will collect a mere load of bricks, many of which he will subsequently drop. To the student destined for medicine or science who wonders why one topic must give place to another just as it becomes really interesting I can recommend only patience. If he is medical, I hope he may have the opportunity of indulging his curiosity in an additional year's study and that he may put his knowledge to good use later on. If he is a pure scientist he may look forward to his final year.

RESEARCH

In comparing physiology with other sciences I said that the parent, medicine, exacted a tribute from her offspring. That was a rather frivolous way of introducing one of the most important characteristics of physiology. Not only medicine but also physiology is a jealous parent, and in a more significant way than the one just discussed. In other sciences the exploration of new fields can be an end sufficient unto itself. The investigator, as he is fond of pointing out, asks how but not why. The meaning underlying the phenomena of the physical universe is left to philosophers to think about, and, indeed, they do not always welcome the ideas of the amateur. Though on the largest scale physiology is but one of the branches of knowledge on which philosophers reflect, on a smaller scale it may be recognised as the study of a world within the world. The human or animal body is a recognisable unity—a part of larger units, it is true, but nevertheless a unity in itself, with sufficiently well-defined physical boundaries.

Now, however absorbing and abstruse are the problems of how a nerve-fibre transmits excitation, or how a muscle contracts; however many years of his life a man may devote to studying the physical and chemical properties of the red blood-cell; the story always seems incomplete until the question is answered: "What does this mean to the individual as a whole?" Man is, indeed, fearfully and wonderfully made, as the anatomist, the histologist, the chemist, and the physicist can testify. In so far as these explore the processes of life, their investigations are physiological. But what may be termed the characteristically physiological outlook is dominated by the question of how the infinity of structural and functional refinement found in the body is mobilised so as to work harmoniously and preserve the integrity and identity of the individual. In other words, the physiologist, though often self-consciously and with a degree of circumlocution, asks not only how but also, in a limited sense, why. At the back of his mind is always the question: "What is the purpose of this process, this reaction, or this adjustment?" Or, as he is more likely to put it: "What is its value to the animal?"

The fulfilling of a purpose is not, of course, admissible as an argument even in the restricted sense in which I am now using the word. A physiological hypothesis must stand or fall by the ordinary rules of scientific evidence. But there is no doubt that it affects the relationship of the research-worker to his problem. The coördinating of his findings with those of his colleagues, the feeling that, while his job is to work on one corner of the canvas, he must keep an eye on the whole picture, is of more immediate concern to him than to those who work in the physical sciences. Though he is not permitted to say that his findings must be right if they reveal something which works to the advantage of the organism, he would probably feel impelled to explain away anything which appeared to operate to its hurt.

Medicine embraces the study of not only the individual but also of the individual in conflict with his environment; and not only the physical but also the mental aspects of the conflict. There can be no doubt that, apart from its utilitarian aspects, medicine is a study of the greatest cultural importance. It is satisfying in that it can exercise possibly the highest, at all events a greater range, of the qualities of the human mind than almost any other study. In an essay on the function of criticism in medicine F. M. R. Walshe remarks[1] that this is:

> "a time when the climate of opinion does not favour the critical, and when interest has swung from any living conception of medicine and physiology as branches of natural philosophy to a predominant preoccupation with new techniques and their rich harvest of new facts. That the harvest is rich it would not be candid to deny."

It is indeed important that, in this age of disillusionment and, what is worse, exploited disillusionment, we remember, while ever more assiduously seeking new facts and new techniques, that as members of a university we seek also in some degree to discover the utmost significance of these facts. It is fashionable to regard the social function of science and the social function of medicine in a material light, but the patient looks instinctively to his doctor for more than a bottle of medicine, and the public looks to the university for more than a supply of medical technicians. It is the share borne by the scientist and the physician in the pursuit of knowledge, their conscious attempt to come at some point into contact with the deepest intellectual problems, and their later function of forming a local nucleus of culture, which justify their presence in the university.

The very qualities of physiology and medicine which appeal to the synthesising and integrating functions of the mind raise philosophical questions which, as foreshadowed by John Theodore Merz,[2] have their practical aspect. He wrote:

> "But biology is not only a subject of purely scientific interest. There is a second and larger class of students—those who study biology as the basis of the art of healing, the medical profession. To them the question of life and death, of the normal or abnormal coöperation of many processes in the preservation of health or the phenomena of disease, is of prime interest; the knowledge of the mechanical, physical, and chemical properties and reactions of living matter, of the construction of the organs and their functions, is only the means to an end. Before the time of Lavoisier, with the solitary exception of Descartes, biology was studied only by medical men; indeed to them both the existence and the progress of the science were entirely due. For them the paramount questions must always be, 'What is life? What is its origin? What is death? What are its causes? What is disease?' To this class of students we are indebted for again and again bringing forward and trying to answer these fundamental, these central questions.
>
> "By the other, the smaller yet increasing class of purely scientific biologists, we are being continually told that these questions are premature or metaphysical, and that the answer we may give to them is of no scientific importance and of no scientific value. The questions 'What is electricity? What is the ether?' cannot yet be answered; nevertheless the sciences which deal with the properties of the ether or of electrical bodies are advancing daily. So also—we are told—does the science of biology progress, even though we leave the question 'What is life?' unanswered. This would be a tenable position if the living organism were like an electrical or an optical

1. Walshe, F. M. R. Critical Studies in Neurology. Edinburgh, 1948.
2. Merz, J. T. History of European Thought in the Nineteenth Century. Edinburgh, 1904–12; vol. II, p. 379.

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apparatus, constructed by man himself with the modicum of knowledge which he possesses. But the living organism, the eye that can see or the nervous system that is in action, or even the smallest 'autonomous' cell, visible only with the microscope, are each an apparatus constructed by nature with the employment of all the intricate agencies which are at her command. In dealing with such an apparatus, we are again and again tempted to ask, 'What is life?' On what does the normal and healthy coöperation of all parts in the living organism depend? In what does it consist?' Fragmentary knowledge may be well enough so far as it goes, but every medical practitioner must painfully feel it to be altogether insufficient. Where practical interests are involved we cannot indefinitely postpone our answers. Science can wait and content itself with the known and the knowable. Practice is face to face with the unknown and the unknowable. Thus the question will again and again be asked 'What is life?' And for the benefit or injury of mankind theories will exist which profess to handle this delicate problem successfully, even as weather-prophets will always exist though necessary knowledge for accurate prediction is still wanting."

Implicit in the last sentence is the warning that to rest satisfied with purely intuitive interpretations is dangerous, inevitable though these may be in practice. In this connexion the state of medicine, just over a hundred years ago, as described by Helmholtz,[3] the famous physicist and physiologist, is illuminating:

"My education fell within a period of the development of medicine when among thinking and conscientious minds there reigned perfect despair. It was not difficult to understand that the older and mostly theorising methods of treating medical subjects had become absolutely useless. But with the theories the facts which underlay them were so indissolubly entangled that these too were mostly cast overboard. How the science must be newly built up the example of the other natural sciences had made clear, but yet the new task stood of giant height before us. A beginning was hardly made, and the first beginnings were often very crude. We cannot wonder if many honest serious thinking men then turned away in dissatisfaction from medicine, or if they from principle embraced an extreme empiricism."

Elsewhere[4] Helmholtz said:

"The vitalistic physician considered that the essential part of the vital processes did not depend on natural forces, which, doing their work with blind necessity and according to a fixed law, determined the result. What these forces could do appeared quite subordinate, and scarcely worthy of a minute study. He thought that he had to deal with a soul-like being, to which a thinker, a philosopher, and an intelligent man must be opposed. . . .

"At this time auscultation and percussion of the organs of the chest were being regularly practised in the clinical wards. But I have often heard it maintained that they were a coarse mechanical means of investigation which a physician with a clear mental vision did not need; and it indeed lowered and debased the patient, who was anyhow a human being, by treating him as a machine. To feel the pulse seemed the most direct method of learning the mode of action of the vital force, and it was practised, therefore, as by far the most important means of investigation. To count with a repeater was quite usual, but seemed to the old gentlemen as a method not quite in good taste. There was, as yet, no idea of measuring temperature in cases of disease. In reference to the ophthalmoscope, a celebrated surgical colleague said to me that he would never use the instrument, it was too dangerous to admit crude light into diseased eyes; another said the mirror might be useful for physicians with bad eyes, his, however, were good, and he did not need it.

"A professor of physiology of that time, celebrated for his literary activity, and noted as an orator and intelligent man, had a dispute on the images in the eye with his colleague the physicist. The latter challenged the physiologist to visit him and witness the experiment. The physiologist, however, refused his request with indignation; alleging that a physiologist had nothing to do with experiments; they were of no use but to the physicist. Another aged and learned professor of therapeutics, who occupied himself much with the reorganisation of the universities, was urgent with me to divide physiology, in order to restore the good old time; that I myself should lecture on the really intellectual part, and should hand over the lower experimental part to a colleague whom he regarded as good enough for the purpose. He quite gave me up when I said that I myself considered experiments to be the true basis of science." [This referred to about the year 1841.]

"It was one man more especially who aroused our enthusiasm for work in the right direction—that is, Johannes Müller, the physiologist. In his theoretical views he favoured the vitalistic hypothesis, but in the most essential points he was a natural philosopher, firm and immovable; for him, all theories were but hypotheses, which had to be tested by facts, and about which facts alone could decide. Even the views upon those points which most easily crystallise into dogmas, on the mode of activity of the vital force and the activity of the conscious soul, he tried continually to define more precisely, to prove or to refute by means of facts."

The beneficial effects of the renaissance in physiology which started in the early years of the last century under the leadership of Müller and his pupils are very obvious in the light of these reminiscences. The movement rapidly gained momentum, with the help of the then incomparable German university system, and spread to this country and America largely through William Sharpey and his school.

However, the general tenor of the passage quoted from Merz is sympathetic on the whole to those who insist on posing the big question, and the fact must be faced that many are now asking where the flood of new knowledge, which has never checked, is carrying us. F.M.R. Walshe[1] voices these doubts:

". . . Physiology, true to its nature as a branch of liberal knowledge, sees no reason why it should not continue to browse at will upon the rich pastures of uncropped knowledge, giving no thought to any philosophy of knowledge, while medicine, faced by its ultimate purpose, has clamant responsibilities in the ordering of the knowledge at her disposal, and in the maintenance of a balance of activity and thought, that she dare not continue to evade. Medicine, then, has come to see that the unending additions to knowledge call urgently for a corresponding measure of integration. Yet we must try to strike a fair balance in this matter. Let it not be thought that I am making odious comparisons between physiologist and physician. We are both in the same boat, and in medicine we need not flatter ourselves that it is primarily out of any intellectual disquiet, or out of a divine discontent with the chaos of information that lies around us, that we have been brought to realise our dilemma, namely, the necessity and the evil of specialisation. We are as innocent of any philosophy of knowledge as the physiologist. Our concern arises because much that is implied in the term 'specialism' has come to be an obstacle in the teaching and practice of medicine."

A hundred years ago there was despair because the practice of medicine was based on guesswork and tradition. There is consternation today because it is in danger of bursting into fragments from a surfeit of ill-digested knowledge.

Any deliberate brake on the acquisition of new facts is not to be thought of; they represent the raw materials of organised knowledge. What is perhaps needed is that they should be more thoroughly sifted and integrated into more manageable units. Everyone who has followed the development of physiology over a number of years knows that minor generalisations are constantly taking place, and that a confused jumble of original discoveries, reported in ones and twos from all over the world, suddenly becomes sorted out into a straightforward story. The leap forward in understanding thereby achieved takes very little effort to assimilate. This process requires to be accelerated; it does seem that at present there is a tendency for research-workers to get as much ground as they can roughly explored and cleared, without

3. Helmholtz, H. L. F. Popular Lectures on Scientific Subjects. London, 1869; vol I, 346.
4. Helmholtz, H. L. F. *Ibid.* London, 1877; vol II, 218, 221.

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bothering about its cultivation. There are two ways in which this tendency may be corrected.

The first is to deprecate the idea that skill in a specialised branch of physiology relieves the young research-worker from the responsibility of acquiring as much general knowledge as possible. The second is for scientific journals to modify their practice of only accepting contributions which have an experimental basis. It would be a most doubtful policy to encourage professional thinkers—they are born, not made. I am also critical of the introduction of professional organisers of knowledge. What is wanted is a slightly different ideal to replace the enthusiasm for exploration at all costs, which has led to the rather feverish kind of scientific activity which is embarrassing us at the moment.

That is speaking comfortably as a scientist to whom it does not matter greatly how fast or how often generalisation comes. Speaking as a teacher, however, and probably for those engaged in the practice of medicine, one must take a somewhat less complacent view. In the practice of medicine, well-founded new knowledge must be acted on, in fairness to the patient. If the technical procedures involved in the application of this knowledge are elaborate, then more and more specialism cannot be avoided. But, though the practice of medicine may be divided, the patient cannot, and in our day no less than in Solomon's a solution must appear quickly. It is not for me to say what I think that solution will be.

As regards teaching, teachers will in general also be research-workers, and may be responsible for large and flourishing departments. There is no reason to believe that the number of departments will become less, and every reason to suppose that any change will be in the usual direction of an increase in number. No university department is, or should be, so specialised that a thorough study of the subject which it professes is not an education in itself. Students who are specialising may safely be left in the hands of their professor. Medical students, however, pass through a great number of departments, and it is important that the cultural value which I have attributed to medicine (in its broad sense) should not be impaired by completely incoördinated teaching between departments. There are many ways in which this coördination can be brought about which need not involve any loss of departmental sovereignty. It is most gratifying to me to find myself in a university which is attacking this problem in a statesmanlike and, above all, a friendly way. I am certain that the best way in which the permanent members of a university can maintain the freedom to pursue their special activities to the credit of that university is to merge themselves sometimes into unofficial units of a supradepartmental nature if that is necessary to minister more effectively to the needs of their successors in the next generation.

". . . One hears much discussion of the rise of specialists and the decline of the general practitioner. In retrospect it is easy to see what has happened. The rapid development of knowledge which followed the use of the scientific method made it impossible for any man to acquire all the special skills and technics. Furthermore, the narrow view of pathology, engendered by its restriction to those ponderable factors to which the methods of science could be applied, left the general practitioner inadequately prepared to deal with some of the most important aspects of family practice. . . . The only thing we can do under the existing circumstances is to brace ourselves for a fresh start. To begin with, we must make our concepts and teaching of pathology inclusive enough to embody psychopathology and social pathology together with the traditional discipline. At the same time we must revise our clinical curriculum so as to give psychiatry its place in the training of the general physician. Not until we have done that will we have the kind of family doctors we need to deal with all forms of disease at the source."—Prof. W. S. McCann, *Med. Ann. Dist. Columb.* 1949, 18, 1.

MEGALOCYTIC ANÆMIAS *

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(*Concluded from p. 296*)

FOLIC ACID

Spies et al. (1945) and Moore et al. (1945) described the remarkable effects of giving pteroylglutamic acid, a synthetic folic acid that had been synthesised by Angier et al. (1945, 1946), to patients with nutritional macrocytic anæmia and pernicious anæmia. Since then intense enthusiasm, limited only by the cost and restricted supplies of this synthetic substance, has led to extensive observation on its value in treatment, more particularly in the U.S.A., where many reports have appeared. Early in 1946 we received supplies and tried its effects in small groups of patients with pernicious anæmia and in other conditions (Wilkinson et al. 1946). It is nearly two years since we started these tests, and I have described fully our results with 20 patients with pernicious anæmia (Wilkinson 1947, 1948). Whether it is given by mouth (10–20 mg. daily) or parenterally (50–200 mg.), the effects are practically the same—there is usually a prompt reticulocytosis, with a rapid rise in the red-cell count, hæmoglobin percentage, and, in some cases, the white-cell and platelet counts. In most patients the counts approach normal values, though macrocytosis tends to persist. Ultimately, however, many of the patients require increasing doses of pteroylglutamic acid to prevent relapses. Some patients relapse severely, a few do not respond at all, and some may remain quite well. With the improvement in the hæmopoietic condition the clinical improvement is very good, but glossitis may persist intermittently and even recur. Nevertheless it is clear that "folic acid" is not so good as liver and stomach therapy, which produce and maintain complete remissions if given properly.

NEUROLOGICAL CHANGES

In evaluating any new treatment for pernicious anæmia the greatest interest lies in the effects on the neurological changes. The results up to January, 1948, obtained with pteroylglutamic acid are extremely disconcerting and disappointing in certain important respects. In my series 4 of the 21 patients had early subacute combined degeneration of the cord before treatment; after folic-acid therapy was started 1 of these showed no improvement, the other 3 became worse; and 5 others (making 9 in all), originally free from neurological changes, rapidly developed in two or three months acute symptoms and signs of subacute combined degeneration of the cord in spite of a very good hæmatological improvement. None of these cases improved on increased doses of pteroylglutamic acid, but liver and stomach preparations are now leading to some relief. The acuteness of the onset of neurological symptoms is something that I have never seen before with any other form of treatment; nor, so far as I am aware, have others. In fact it almost seems that folic acid has a specific effect in producing or precipitating the spinal-cord degeneration. The simultaneous administration of liver extract with folic acid merely delays the onset but does not prevent it.

Similar observations are being reported from other clinics, and up to now I have collected from the published reports records of neurological changes developing for the first time or worsening in 60 patients (acute or fulminating in 9) out of 184 cases of pernicious anæmia treated with synthetic pteroylglutamic acid. On the other hand, pteroylglutamic acid may be of use in the treatment of other conditions, provided there is a megalocytic anæmia with a megaloblastic marrow.

* The Oliver-Sharpey lectures delivered at the Royal College of Physicians of London on March 9 and 11, 1948.

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Though such conditions as sprue, cœliac disease, and idiopathic steatorrhœa give irregular results, nevertheless, when associated with megaloblastic marrows, they, in common with megaloblastic anæmia of pregnancy, nutritional megalocytic anæmias, and, possibly, achrestic anæmia—all with megaloblastic marrows—may respond very well. If the bone-marrow shows a normoblastic reaction in these conditions as with other non-megaloblastic blood diseases, pteroylglutamic acid is of no value in therapy and should not be used.

However, it is clear that folic acid must not be used, in fact is definitely contra-indicated, in the treatment of pernicious anæmia, whether or not neurological symptoms are present—for the reasons already given. There is no justification whatsoever for the manufacture of blunderbuss mixtures of folic acid with liver, stomach, and other constituents which, irrespective of their greater cost, do not contain adequate quantities of their respective constituents and constitute misleading and dangerous therapy for pernicious anæmia.

PROGNOSIS IN PERNICIOUS ANÆMIA

Many will remember the very poor outlook for patients with pernicious anæmia before the introduction of liver diet. As an illustration from my own records, of the last 68 patients who, before liver diet was introduced, were treated with iron, arsenic, blood-transfusion, &c., 36 (53%) died within four weeks of diagnosis in hospital, 59 (85%) died in less than twelve months, 8 within a further seven months—i.e., 95% dead in nineteen months—and 1 lived for four years—for the whole group an average duration of life of six months from the date of admission to hospital (Wilkinson and Brockbank 1929). The prognosis was completely altered by Minot's introduction of liver diet in 1926, and with the development of hog's-stomach treatment in 1929 I reported the excellent therapeutic results we obtained, surpassing those with the liver treatment (Wilkinson 1930, 1931, 1933b and d); these stomach preparations produced more rapid and satisfactory responses than did liver, and I subsequently found that neurological changes improved much more satisfactorily than with oral or parenteral liver extracts.

From that time various types of stomach and liver preparations have been used. My patients after first examination and treatment in hospital are instructed to attend regularly at my follow-up clinic for control and, if necessary, treatment. For the last nineteen years this has worked very well, though during the war it was often difficult owing to the number of patients who were lost through air-raids or for various reasons were dispersed to other areas; some, consequently not attending, did not always get that necessary attention owing to the absence of their doctors.

In my consecutive series of 1600 patients (every one of whom I have seen personally) there were 638 males and 962 females (1 : 1·5); and, when first diagnosed as having pernicious anæmia, their age-distributions were as follows:

	Age-groups (years)					
	20	*21–30*	*31–40*	*41–50*	*51–60*	*61+*
Males	0	14	53	125	220	226
Females	1	31	114	191	304	321
Total	1	45	167	316	524	547

Of these there was only 1 patient under 21 years of age, and only 46 (2·8%) under 30, whereas 1071 (67%) were over 50.

The prognosis for patients with pernicious anæmia has of necessity had to await the passage of time, but it has been my view for many years that, provided the patient is properly and adequately treated with a good preparation of stomach or liver, the prognosis should be excellent—always excluding the possibility of complications or coincidental disease. There is no doubt from our experience that patients attending regularly at a suitable clinic, where control tests can be carried out and treatment supervised, are in far better health and general condition in every way than their contemporaries without pernicious anæmia. The excellent condition of these patients as they get older is most striking. Nevertheless, with the great increase in expectation of life for pernicious anæmia, it is to be expected that these patients will be liable to all the usual illnesses that may arise—infections, influenza, and pneumonia are specially to be feared owing to their profoundly depressant effects on hæmopoiesis—and treatment must be increased at these times. Older people are more liable to conditions such as neoplasm, hyperpiesis, cardiac troubles; hence these will appear in some cases. Of the manifestations of the disease itself perhaps subacute combined degeneration of the cord is the most resistant and troublesome, since the older patients do not readily improve when the severer neurological manifestations are present.

Since 1929, out of 1532 of my patients 1480 have had treatment with stomach preparations or liver (raw or extracts), and there are 1179 still alive, while 301 have died; of the last the duration of life from first diagnosis was less than 5 years in 152 (50·5%) patients, 149 (49·5%) lived for longer than 5 years, 51 (17%) longer than 10 years, and 12 (4%) survived for 16–20 years.

Causes of Death in Pernicious Anæmia

Cancer (non-gastric)	42
Cerebral hæmorrhage and thrombosis	38
Cancer of stomach	28
Pneumonia (lobar, bronchopneumonia)	26
Subacute combined degeneration	21
Coronary thrombosis, mitral disease, auricular fibrillation, pericarditis	18
Pernicious anæmia (treatment refused or discontinued)	17
Cardiac failure (all hyperpietic)	13
Mental disease and suicides	13
Nephritis, uræmia	10
Asthma and bronchitis	6
Pulmonary tuberculosis	6
Fatal accidents	5
Hæmatemesis	4
Diabetes mellitus	3
Myeloid leukæmia	2
Chronic intestinal disease	2
Other miscellaneous conditions	25
Causes of death under inquiry	22

In these 301 out of 1532 patients—i.e., 1600 less the 68 pre-liver era patients who died of pernicious anæmia or subacute combined degeneration of the cord—38 died of cerebral hæmorrhage or thrombosis, 70 of cancer (stomach 28, other sites 42), and 26 of lobar pneumonia or bronchopneumonia. All the 17 (1·1%) who died of pernicious anæmia had either refused treatment or discontinued treatment entirely and died at home.

Of great interest was the extremely rare occurrence of chronic myeloid leukæmia—in 2 patients, both of whom lived for 5 and 3 years after the leukæmia had been diagnosed, and 15 and 8 years after the original diagnosis of pernicious anæmia.

Of these patients 62 had had hyperpiesis (blood-pressure higher than 170/100 mm. Hg), which was almost entirely in patients dying of cerebral hæmorrhage, cardiac disease, or nephritis. The occurrence of hyperpiesis in surviving patients is of great interest. With the passage of time I found that many of my older patients began to complain of headaches, sometimes a little palpitation or dyspnœa, quite inexplicable by their good blood-count. Examination in such cases usually revealed considerable hyperpiesis (the insidious onset of

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these symptoms may be missed in the early stages). In 19% of my series, when pernicious anæmia was first diagnosed, the blood-pressure was over 170/100 mm. Hg, and in 55% below 140/90. On the other hand, including the fatal cases already mentioned, 56% of the treated pernicious anæmias had blood-pressures greater than 170/100, most being over 200/120.

I thought at one time that the liver diet was responsible for this increase in hyperpiesis, but it happens after all forms of treatment, without significant emphasis on any one type; it is still important that anti-pernicious-anæmia treatment should be continued without diminution in spite of this hyperpiesis.

In 4 cases the patients died at home after hæmatemeses. A hæmorrhagic tendency in pernicious anæmia might be expected in severe relapses, for at those times the number of platelets may be very much diminished; but this is very rarely observed. The commonest fatal hæmorrhagic manifestation is cerebral hæmorrhage as the sequel to long-standing hyperpiesis. Other and non-fatal bleedings may take place in the retinæ, often associated with optic atrophy; and hæmaturia and hæmatemeses are occasionally noted. I have had 6 patients report after severe hæmatemeses, but in every case I have not found any cause for them either clinically, gastroscopically, or radiologically.

Now, with the greatly lengthened expectation of life in these patients on fully adequate treatment, other not necessarily fatal diseases are to be expected (Wilkinson 1933c and e). Excluding the occasional sporadic conditions, such as tuberculosis, various dermatoses, venereal disease, allergic conditions, leukæmia, neurological conditions other than subacute combined degeneration of the cord, and so on, we must note cancer, thyroid disease, cardiovascular incidents, and diabetes.

PERNICIOUS ANÆMIA AND CANCER

Malignant disease is usually associated with a secondary microcytic hypochromic anæmia of progressive severity, and only rarely does one see a megalocytic hyperchromic anæmia (with megaloblastic or normoblastic marrow) as a direct consequence of the neoplastic condition. The association of addisonian pernicious anæmia and cancer seems at first sight to arise fortuitously in the small number of cases reported. Of necessity there had been only a relatively small series of cases with the short periods of time since liver and stomach therapy was introduced (Wilkinson 1933c and e). With opportunities of following up larger groups of patients over periods up to twenty years we have perhaps a better chance of considering the relationship of these two conditions.

In the past, and in common with most other observers, I (Wilkinson 1933c and e, 1945) have been inclined to view the association of pernicious anæmia and cancer as possibly coincidental; but, now that my patients with pernicious anæmia are living so much longer, cancer is occurring more frequently. During the last two years I have been looking into the question again. In 1933 I had only seen 8 cases of cancer (2 in the stomach) in 370 patients with pernicious anæmia, and I discussed the rare occurrence of this combination in other reported series. At that time only 30 examples were found in published reports, and non-gastric neoplasms were even more rare, there being only 10 cases reported. Even then, I suggested that, with the increased expectation of life with modern treatments for pernicious anæmia, the frequency of malignant disease might be much increased (Wilkinson 1933c and e), a view that was also held by the late Sir Arthur Hurst. Since then my series of pernicious anæmia has grown to 1600, and I have now seen 70 (4·4%) patients in whom cancer has been present before or after the diagnosis of pernicious anæmia—28 (1·75%) in the stomach, and 42 (2·6%) elsewhere. Of these patients 6 are still alive. The onset of cancer of the stomach was seen 1–17 years (average 7·5 years) after pernicious anæmia was first diagnosed; in 22 patients (8 after 11 years) 5 were diagnosed simultaneously; and 1 developed pernicious anæmia 5 years after a gastrectomy for cancer of the stomach.

The only obvious ætiological factor common to pernicious anæmia and most gastric cancers is the achylia gastrica usually associated with a chronic gastritis. Jenner (1939) reported 8 gastric cancers in 181 patients with pernicious anæmia, and thought that gastritis was the common factor, the frequency of cancer in pernicious anæmia thus being significantly raised. But in recent years the proportion of neoplasms in other sites has increased greatly, now exceeding those in the stomach, and gastritis cannot be claimed as an ætiological factor in these cases, nor indeed in all gastric cancers. Nevertheless, broadly speaking, in pernicious anæmia the achlorhydria, so commonly familial, must be considered as a possible ætiological factor in the development of gastric cancer. Further, 69 (4·3%) of my patients gave a family history of cancer in their relations, and I have previously cited the remarkable family of Borovanská-Felklová (1930), in which a man who died of gastric carcinoma had four sons, of whom the eldest had pernicious anæmia and gastric cancer, two others had pernicious anæmia and the fourth achylia gastrica. Rigler et al. (1945) and Kaplan and Rigler (1947) reported 18 (6·9%) cases of gastric cancer in 259 cases of pernicious anæmia examined radiologically, and 36 out of 293 at necropsy, and claimed that their findings were statistically significant; but fallacies may arise from restrospective diagnosis of pernicious anæmia even in necropsy material. Recently Bourne (1948) has reported 3 cases of gastric carcinoma in a group of 15 symptom-free patients with pernicious anæmia re-examined gastroscopically and radiologically ten years or more after diagnosis. My series produced 28 gastric cancers in 1532 patients who lived—i.e., 1·83%, or on the basis of total fatal cases (28 gastric cancers in 301 dead pernicious-anæmia patients) a frequency of 9·3%—and therefore suggests the necessity for regular and frequent examination of all patients with pernicious anæmia.

DIABETES

Though only 3 patients died of diabetes in my series there were 33 (2·1%; 15 males, 18 females) with both diseases. Of these, 15 had diabetes and pernicious anæmia diagnosed simultaneously, 13 developed diabetes subsequently (8 in less than 5 years, 3 in 5–10 years, and 1 each in 11 and 17 years), and 5 had had diabetes for 1, 3, 5, 10, and 12 years before pernicious anæmia was found. Of these patients 8 have died, but only 3 of the diabetic condition (the other deaths were due to tuberculosis, accident, suicide, and nephritis), and all had their last blood-counts within normal limits. Treatment was well controlled with liver or stomach for the anæmia, and with insulin (11 cases) or diet without insulin (22) for the diabetes. The 25 living patients are in good health now—2 are over 80, 13 over 70, and 12 between 41 and 70 years of age.

Achlorhydria has been noted in diabetes in many different reported series of patients in a frequency varying from 29 to 49% of cases examined (Oliver and Wilkinson 1933). Here again the question arises whether achlorhydria is a common ætiological link between the two conditions—certainly I have noted the frequent familial occurrence of pernicious anæmia or of diabetes in the relations of such patients. Bowen and Aaron (1926) suggested that achlorhydria was only seen in severe diabetes of more than a year's duration, and was a secondary effect due to the diabetes. These patients tend to be abnormally sensitive to insulin (Oliver and Wilkinson 1933).

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THYROID DISEASES AND PERNICIOUS ANÆMIA

The frequent association of thyroid disease, especially hyperthyroidism, with achlorhydria (up to 80% in some series) has previously been considered (Oliver and Wilkinson 1933), and Berryhill and Williams (1932) suggested that the thyroid overactivity might play a major rôle in reducing the secretion of acid and pepsin. This achlorhydria may precipitate pernicious anæmia but does not explain the development of hyperthyroidism years after pernicious anæmia has been noted. Numerous observers have described odd cases; Giffin and Bowler (1923) found 5 in 628, I found 6 in 370, which increased to 33 in 1600, Meulengracht (1929) found 8 in 151, and so on; whereas others have not seen any. The association of achlorhydria and myxœdema with pernicious anæmia is seen much less often than with microcytic hypochromic anæmia, which is often seen in familial relationship to pernicious anæmia (see above).

Among my cases of pernicious anæmia 42 patients had a disorder of the thyroid gland: 33 exophthalmic goitre or toxic hyperthyroidism; 7 myxœdema; and 2 simple goitre. In this group there is a striking preponderance of 36 females to 6 males (3 with toxic hyperthyroidism, 2 with myxœdema, and 1 with simple goitre). Diagnosis of thyroid disease was made in 19 cases before pernicious anæmia was diagnosed, in 16 simultaneously, and in 5 (2–14 years) after pernicious anæmia was observed.

PERNICIOUS ANÆMIA WITHOUT OTHER COMPLICATING DISEASES

Now let me turn to the present position with modern treatment for the remainder of my patients with pernicious anæmia. In January, 1948, I have still alive 1179 patients on stomach or liver therapy, including 1 patient of 100 years of age, 7 over 90, 99 over 80, and 396 over 70 (232 females and 164 males—i.e., 1·4 : 1). These patients, who are taking either hog's stomach in doses varying between 30 g. daily and 3·5 g. on alternate days, or liver as oral extracts (1 drachm to ½ oz. daily) or intramuscular preparations (1–2 ml. every 1–3 weeks) are in very good health, most of them free from neurological symptoms, but some with various degrees of residual cord involvement, peripheral neuritis, or minor paræsthesiæ. Excluding those treated with folic acid, none has become worse on treatment. In general health they compare more than favourably with contemporary non-anæmic people.

Of these 1179 patients in good health, 1032 (87·5%) have been treated for more than 5 years, 760 over 10 years, 283 over 15 years, 41 over 20 years; 2 are alive after 25 years, and 1 after 32 years from the time of original diagnosis.

CONCLUSION

As a result of investigations in the last twenty-two years the entire outlook for many patients with megalocytic anæmias, particularly pernicious anæmia, has completely changed.

Pernicious anæmia, which was and still is invariably fatal if untreated, can and should be adequately controlled by appropriate treatment to give healthy, often normal, lives to those affected. Further, provided that adequate treatment is given with active anti-anæmic preparations, none should fail to respond and keep well for at least the normal expectation of life.

Regular and careful supervision both clinically and hæmatologically, preferably in special clinics, should prevent, or detect in the early stages, complications requiring additional treatment.

No patients should die of pernicious anæmia or develop subacute combined degeneration of the cord if only they are treated sufficiently early, vigorously, and persistently. This requires the fullest coöperation and understanding on the part of the patient, the doctor, the manufacturer of anti-anæmic preparations, and the clinic.

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EFFECT OF ANALGESICS ON RESPIRATORY RESPONSE TO CARBON DIOXIDE IN MAN

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ANALGESIC drugs pharmacologically similar in action to morphine all cause some depression of respiration. This fact is of great importance in obstetric practice and to a less extent in the treatment of aged and infirm patients. Great care, for example, is needed in the use of morphine in obstetrics owing to its depressant effect on respiration in the newborn.

Investigations on analgesics have been made in these laboratories with the object of producing a drug in which the respiratory depressant effect is small, analgesia is efficient, and undesirable side actions are reduced. All drugs prepared here have been tested for respiratory depressant activity on rabbits, and many of these results have been reported in brief by Thorp et al. (1947a and b) and Thorp (1948).

The method consists of continuously recording the respiratory volume per min. of unanæsthetised rabbits before and after subcutaneous injection of the drugs under examination.

In all cases where the drug proved sufficiently interesting an attempt was made to establish a dose/response relationship for the respiratory depressant action, and to compare the doses of different analgesics producing equivalent degrees of respiratory depression.

This method is open to several objections, principally owing to the use of larger doses of the drugs than are required to produce adequate analgesia, with the result that the respiratory depressant action may have a mixed physiological origin. It has also been felt that a measurement of this effect in man should precede any clinical trials on patients or expectant mothers. The rabbit method has, however, proved useful in eliminating drugs unlikely to be of value and in indicating those worthy of further trial.

Linhard (1911) showed that morphine depresses the response of the respiratory centre on stimulation with carbon dioxide, and this was confirmed by Henderson and Rice (1939), using a different experimental approach. These workers concluded that the effect of morphine is similar to a reduction in the concentration of carbon dioxide in the inspired air.

Some of the factors influencing the relationship between the respiratory volume per min. and the concentration of carbon dioxide inhaled were investigated

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by Padget (1928), who showed that there is a quantitative correlation between the stimulus and the response, and that, though the response varies from person to person, the effect on any one person is constant when the experiment is repeated. Padget also showed that whether the person was resting or had recently taken exercise made little difference to the response obtained.

Our experiments were made on male and female volunteer medical students during three college vacations. Since such experiments took up a considerable time, only a selection of typical analgesics and the most promising of the newer synthetic compounds could be examined.

METHOD

Two complete sets of apparatus were set up in a quiet room, and four volunteers were used at a time. The apparatus consisted of a Gaddum (1941) respiration-recorder designed for use in man and arranged for ink writing on glazed kymograph paper. The outlet of the bottle of Gaddum's flow-meter was connected by corrugated hose to a British Service respirator face-piece (mark v), modified by removing the inlet valve from the top of the canister and inserting it in the air inlet of the face-piece. This mask is comfortable and very efficient in cases where the fairly large dead-space is of no importance. The inlet of the bottle was connected via a two-way tap either to free air or to a 100 litre Douglas bag containing the gas mixture.

The gas mixtures, obtained from the British Oxygen Company, were the normal 5% mixture of carbon dioxide in oxygen used for resuscitation and a mixture containing 3% of carbon dioxide specially prepared.

The respiration-recorders were calibrated by connecting a vacuum pump and standard flow-meter in place of the volunteer. The recorders could thus be arranged to give approximately linear readings from 5 to 30 litres per min., corresponding to a height of about 1–12 cm. deflection on the kymograph paper. The damping of the recorders was

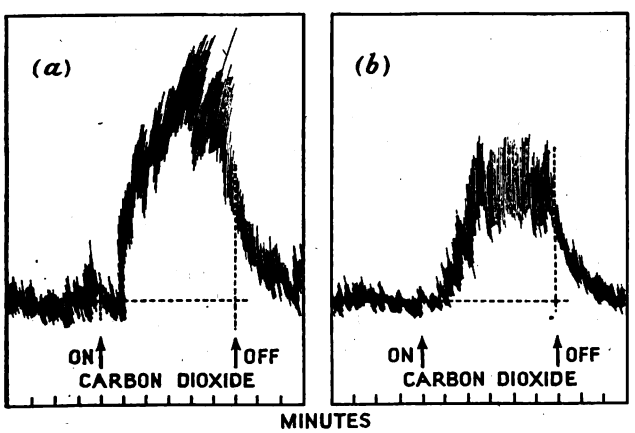

Fig. 1.—Typical records obtained with Gaddum's respiration-recorder in a normal man (case 1): (a) initial response; (b) response half an hour after intramuscular injection of amidone 10 mg.

arranged so that the pointer excursion with each breath was not more than 1 cm. under basal conditions and 3 or 4 cm. at the maximum excursion produced by breathing carbon dioxide.

Each recorder was set up behind the heads of two beds, so that the tube to the face-piece could be interchanged between the two volunteers. The volunteers were allowed to rest on the beds for $^1/_2$–1 hour before the experiments were started. After preliminary experiments the following time-cycle was found most convenient.

The resting subject was connected to the recorder and a resting record taken for 5 min. The tap was then turned to the gas mixture for 6 min., after which the subject breathed air for a further 4 min. This whole cycle lasted 15 min.; hence two subjects could be used on each recorder, taking records every half-hour.

The analgesics were all injected intramuscularly as solutions in physiological saline after an initial record had been taken. Subsequently records were taken every half-hour for $3^1/_2$ hours.

The volunteers were either kept in hospital all night or taken home, and they did not attend again until 2 days later. During the experiments a light meal of tea and toast was provided.

The records were examined in various ways, but the most satisfactory method was to measure the area enclosed by a continuation of the resting respiratory volume per min., the trace formed by the flow-recorder,

TABLE I—RESULTS PREVIOUSLY OBTAINED IN ANIMALS WITH THE ANALGESICS TESTED IN MAN

Drug	Analgesic activity ratio	Respiratory depressant ratio	Strength of solution used in man (mg./ml.)
Morphine ..	1·0	1·0	10
Pethidine ..	0·15	0·15	50
Amidone ..	1·3	1·4–2·0	10
Isoamidone ..	1·0	0·4–0·7	10
Höchst 10582 ..	0·5	0·5–0·7	20
29C48	0·8	0·25–0·3	12·5

and a vertical line from the base-line 6 min. after the start of inhalation of the gas mixture. Two typical records are shown in fig. 1, in which the area measured has been indicated. This area, measured with a planimeter is proportional to the volume of gas breathed during the 6 min. exposure to the mixture and therefore indicates the sensitivity of the respiratory centre.

Observations of the blood-pressure and of any side actions worthy of note were made throughout each experiment.

DRUGS INVESTIGATED

The established analgesics, morphine and pethidine, were used as standards of comparison, and the drugs examined were 'Amidone' (*dl*-2-dimethylamino-4 : 4-diphenyl heptan-5-one), developed by I. G. Farben workers at Höchst during the war and already widely used in Britain and United States as an analgesic; 'Isoamidone' (*dl*-1-dimethylamino-2-methyl-3 : 3-diphenyl hexan-4-one), which has been described chemically by Easton et al. (1947) and tried by Gentling and Lundy (1947) on patients; 'Höchst 10582' (*l*-dimethylamino-3 : 3-diphenyl hexan-4-one); and a new compound '29C48' (*dl*-piperidino-2-methyl-3 : 3-diphenylhexan-4-one), the piperidyl analogue of isoamidone.

All these new compounds were synthesised for this research by Mr. P. Ofner, of the Wellcome Chemical Works, Dartford.

Table I gives the equivalent analgesic potencies determined by Thorp's (1946) method in the rat, and the relative respiratory depressant ratios determined in rabbits.

The doses given to the human volunteers were based on the rat analgesic ratios, which had previously been shown to correlate closely with the values obtained for established analgesics as a result of extensive clinical experience, and were therefore expected to produce an equivalent degree of analgesia.

All these drugs were compared in the same 8 volunteers, so the results could be submitted to statistical assessment designed to take advantage of this feature. A few of the earlier experiments in this research were made on another group of 13 male volunteers, but these were not sufficiently well planned to give a large number of observations with each treatment or to eliminate the variation between persons. The results obtained were used as a guide in the more comprehensive experiments,

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but were not regarded alone as worthy of elaborate statistical analysis.

RESULTS

In the earlier experiments two mixtures, 3% and 5%, of carbon dioxide in oxygen were used to investigate the relationship between the concentration of the gas and the alteration in the sensitivity of the respiratory centre caused by analgesics. It was found that, though the response to carbon-dioxide stimulation was twice as great on inhalation of 5% as of 3% carbon dioxide, the same relationship held after treatment with any of the analgesics examined. A similar percentage reduction of the response, therefore, is caused by the same drug treatment with either carbon-dioxide concentration. The results, expressed graphically in fig. 2, were obtained by taking the mean values of the response to breathing the gas mixtures for the 1/2 hr., 1 hr., and 1 1/2 hr. recordings after injection of the analgesics. These values were then expressed as a percentage of the response obtained before the administration of the drug with the 5% gas mixture. It will be seen that the pairs of curves are parallel but that the one obtained after the drugs had been given is uniformly lower than that in the untreated person.

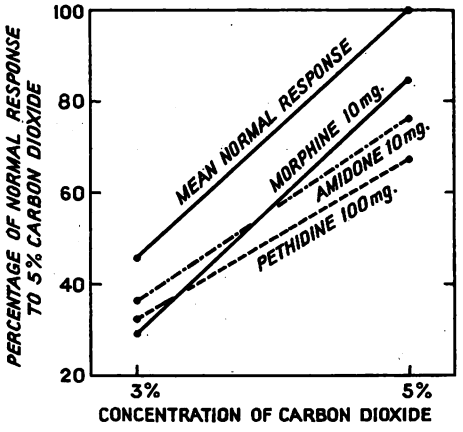

Fig. 2—Results obtained with two concentrations of carbon dioxide before and after the injection of typical analgesics.

On this evidence it was decided to use the 5% mixture of carbon dioxide in oxygen, since there would be less error in the measurement of the response.

Table II gives the mean percentage of the normal response to carbon dioxide obtained at half-hourly intervals for the same 8 subjects when treated with the different analgesics. The results are also shown graphically in fig. 3. It will be seen that the depression of the response falls into two main classes, the three drugs morphine, pethidine, and amidone forming one class and causing similar degrees of depression with equivalent analgesic doses. The remaining three drugs depress the respiratory response only slightly. The differences between the curves at each half-hour have not been tested for statistical significance, but these curves can be of value to indicate the relative duration of the depressant action and the comparative extent of the effect at any time. For a more reliable estimate of the relative respiratory depressant activity of the different drugs the same figures were used to calculate the mean integrated percentage depressions of the response over three and a half hours. For this purpose only depressions of the response were included, so values above the initial response were regarded as 0% depression. The sums of the percentage depression of the response at each half-hour for each person were calculated and the value obtained for the mean of the 8 subjects for each drug together with the standard error of this value.

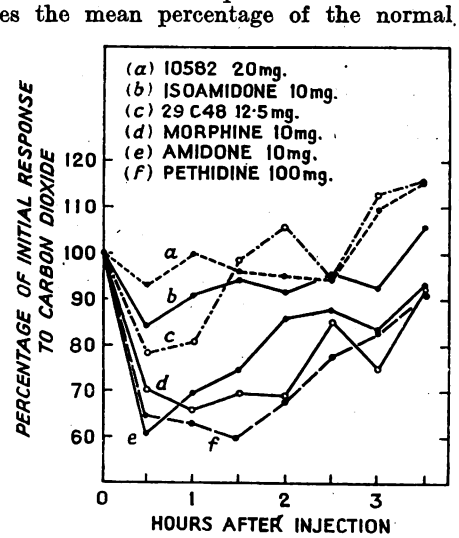

Fig. 3—Responses obtained by inhalation of 5% carbon dioxide in oxygen at various times after the injection of analgesics.

The results, interpreted in this way, are compiled in table III and shown graphically in fig. 4. This method of calculation is equivalent to a measurement of the area bounded by the curves of fig. 3 and below the normal response line at 100%. The values obtained therefore represent the comparative degrees of respiratory depression in each case. The significance of the differences between these figures is also higher, since such differences are summated throughout the experiment. This method of analysis can only be complementary to the graphs of fig. 3, since it gives no indication of the intensity/duration relationship. Fig. 4 shows that in equivalent analgesic doses compound 29C48 was appreciably less depressant than any of the other drugs, and that even at twice this dose it was still very similar in effect to isoamidone and Höchst 10582. These drugs, again, are much less depressant than the group comprising morphine, pethidine, and amidone.

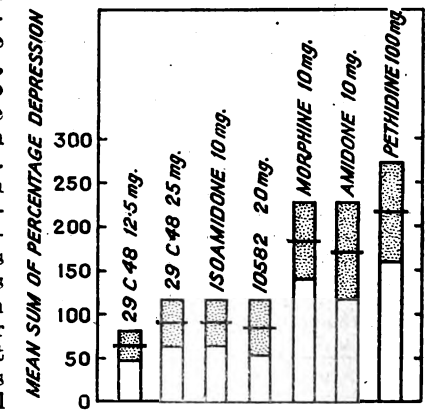

Fig. 4—Depressant actions of analgesics on response to inhalation of 5% carbon dioxide in oxygen. (Based on the analgesic estimations in rats, the smaller dose of compound 29C48 is equivalent to the doses of the other analgesics tested.)

How closely these results correlate with the depression of the respiration of newborn infants will only be established by clinical trials. So far it seems from the work of Prescott and Ransom (1947) that amidone is almost as depressant as morphine, and that, of more established drugs, pethidine is the most useful obstetric analgesic. If the clinical results parallel the results reported above, it is expected that isoamidone, Höchst 10582, and 29C48 will prove greatly superior to pethidine.

ASSOCIATED SIDE ACTIONS

A factor of considerable importance in obstetric analgesia is the general narcotic and sedative effect such drugs produce. The volunteers were therefore carefully observed during the experiments and questioned next day, and the following general observations were made about these drugs:

Morphine.—All the volunteers were depressed and sleepy after the administration of 10 mg. of morphine. Shortly after the injection there was a sensation of warmth and flushing, followed by coldness. Two subjects vomited, 2 felt faint at the end of the test, and 2 complained of a "hangover" next morning. The changes in blood-pressure and pulse-rate were variable and insignificant. Slight slowing of the pulse occurred in 4 persons, and changes of about ± 15 mm. Hg in the systolic blood-pressure were noted in 4.

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TABLE II—MEAN PERCENTAGE OF RESPONSE TO INHALATION OF 5% CARBON DIOXIDE IN OXYGEN AFTER INJECTION OF ANALGESIC DRUGS. EACH FIGURE IS THE MEAN OF 8 OBSERVATIONS. THE SAME PERSONS WERE USED FOR EACH DRUG

Drug	Dose (mg.)	Percentage of normal response to 5% carbon dioxide						
		½ hr.	1 hr.	1½ hr.	2 hr.	2½ hr.	3 hr.	3½ hr.
Morphine ..	10	70·0	65·5	69·3	68·6	84·8	72·4	91·4
Pethidine ..	100	64·2	62·8	59·4	67·6	77·1	80·0	90·8
Amidone ..	10	60·8	69·4	74·1	85·1	87·1	82·0	92·2
Isoamidone ..	10	84·0	90·5	94·0	91·0	94·5	91·5	105·0
Höchst 10582	20	92·8	99·7	95·6	94·8	93·8	108·6	114·1
29C48 ..	12·5	78·0	80·5	98·0	105·0	94·0	112·0	114·0
29C48 ..	25	80·0	88·5	92·0	101·0	98·0	105·0	112·0

Pethidine.—Flushing and sweating developed shortly after the drug was injected. All the volunteers were sleepy or drowsy, and several were euphoric. Euphoria appears to be a characteristic effect of pethidine. Dizziness on trying to walk was common, and 2 persons vomited. A rise of 6–30 mm. Hg in systolic blood-pressure was observed in all subjects. The blood-pressure is generally considered to fall in patients confined to bed, but Gallen and Prescott (1944) recorded a rise of 10–20 mm. in systolic blood-pressure in 150 patients receiving pethidine in labour. The rise is transient and rarely lasts longer than 30–60 min.

Amidone.—The most notable side-effects were nausea and vomiting, particularly when the subjects were walking about after the test; this occurred in 4 persons. Three complained of a hangover lasting until next morning. Dizziness on walking or even on standing up was common. The subjects were not sleepy or mentally depressed. Most of them were reading during the tests. Euphoria was not observed, possibly because of the absence of sedative effect. The changes in systolic blood-pressure (± 10 mm. Hg) and pulse-rate were insignificant.

Isoamidone.—The effects observed were quite unlike those of amidone. No side-effects were experienced, and changes in blood-pressure and pulse-rate were slight. None of the volunteers vomited or had nausea, nor were there complaints of dizziness or after-effects.

Höchst 10582.—This drug also had no side-effects, except for faintness in one person. A slight rise of systolic blood-pressure (up to 10 mm. Hg) was noted in 3 persons. There were no unpleasant after-effects.

29C48.—No side-effects were observed after the administration of 12·5 mg. A dose of 25 mg., however, produced flushing, sweating, a sensation of warmth, dizziness, and euphoria, but these symptoms were not so pronounced as with morphine, pethidine, or amidone. Two subjects also vomited several hours after getting up, and one complained of nausea. No significant cardiovascular changes were observed after 12·5 mg. or 25 mg. Several patients in labour have since been given 25–125 mg. of 29C48 with no unpleasant effects.

DISCUSSION

With a given drug the incidence of side-effects in tests on healthy volunteers is usually much greater than in patients confined to bed, who tolerate the drug much better. The volunteer feels no ill effects so long as he rests in bed—indeed, he is often euphoric and happy—but as soon as he gets up he may note such side-effects as dizziness, weakness, nausea, and vomiting. These are probably due to vasomotor changes resulting from the upright position and resemble the symptoms of vasomotor collapse produced by administering nitrites to healthy ambulant persons.

It will be observed that the least depressant drugs—i.e., 29C48, isoamidone, and Höchst 10582—had the fewest side-effects. These three drugs were not assessed clinically, and perhaps the doses selected were not equianalgesic with morphine, pethidine, and amidone in man, though on the basis of the Hardy, Wolff, and Goodell test (Thorp 1946) and the ischæmic-pain test (Hewer and Keele 1947) they appear to be so. It might be argued that 29C48, isoamidone, and Höchst 10582 are more rapidly excreted than the other drugs and that recovery from respiratory depression soon takes place. This would not explain the slight depression observed with these three drugs in the first half-hour after their injection.

In view of the relative absence of side-effects and the very slight respiratory depressant effect of 29C48, clinical trials are in progress with this drug to see if it has a place in obstetric analgesia. Trials have already been made in obstetrics with Höchst 10582. This drug has no depressant effect on the newborn, but it has the drawback that its duration of action is very short.

The reduction of the sedative, narcotic, and respiratory depressant actions in the newer analgesics has shown that these effects can be separated from analgesic action, but no compound has yet been reported which can specifically abolish the sensation of pain.

SUMMARY

Several analogues of amidone (2-dimethylamino-4 : 4-diphenyl hexan-5-one) were tested to see if they depressed

TABLE III—INTEGRATED VALUES OF DEPRESSIONS OF RESPONSE TO CARBON-DIOXIDE STIMULATION CAUSED BY ANALGESICS

Case no.	Sums of percentage depressions at each half-hour						
	29C48 12·5 mg.	29C48 25 mg.	Isoamidone 10 mg.	10582 20 mg.	Morphine 10 mg.	Amidone 10 mg.	Pethidine 100 mg.
1 ..	70·9	83·5	97·4	70·8	255·8	363·9	272·8
2 ..	158·3	74·8	..	15·6	..	102·8	30·7
3 ..	46·0	150·3	21·3	70·8	115·1	251·8	229·8
4 ..	19·5	16·8	11·5	229·0	393·9	407·9	496·8
5 ..	4·8	245·1	138·5	11·6	120·4	12·7	31·8
6 ..	103·1	1·2	163·4	37·0	108·0	67·1	89·3
7 ..	73·6	77·1	135·3	30·6	172·4	31·6	224·4
8 ..	40·9	80·7	158·6	207·6	278·4	104·5	306·2
Mean	64·6	91·2	90·8	84·1	180·5	167·8	210·2
Std. error of mean ..	17·4	27·2	24·5	30·4	43·6	54·1	55·8
Ratio of means (morphine = 1) ..	0·358	0·505	0·503	0·466	1·000	0·929	1·165

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the respiratory centre in normal human volunteers. The method used was based on the depression of the increase in respiratory volume per min. caused by the inhalation of a 5% mixture of carbon dioxide in oxygen.

Morphine and pethidine were included for comparative purposes, and the results obtained were compared with those previously obtained with larger doses in rabbits.

Though the effects in man and the rabbit were roughly parallel, small differences in the degree of respiratory depression were more clearly demonstrable in man.

Morphine, pethidine, and amidone depressed respiration much more than did isoamidone, Höchst 10582, and a new compound, 29C48 (*dl*-piperidino-2-methyl-3 : 3-diphenylhexan-4-one).

Of all the compounds tested, 29C48 caused the least respiratory depression in man and the rabbit.

The effects on pulse-rate and blood-pressure together with associated side actions are described.

Our thanks are due to those medical students of University College Hospital Medical School who coöperated in this work; Professor Nixon, who provided facilities; Dr. C. A. Keele and Dr. A. S. V. Burgen, of the Middlesex Hospital Medical School, who, with their students, were of considerable help in making preliminary observations on the technique; and Mr. J. B. Attlesey and Mr. R. F. Sellar for their valuable technical assistance.

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URINARY SCHISTOSOMIASIS TREATED WITH MIRACIL D

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'MIRACIL D' is the hydrochloride of 1-methyl-4-beta-diethyl-aminoethylaminothio-xanthone, which German workers have shown to have a therapeutic effect in schistosomiasis in laboratory animals. Hawking and Ross (1948) investigated the toxicity of the drug in animals and human volunteers, and concluded that the maximal tolerated dose for repeated administration was about 0·2–0·3 g. a day. Based on this dosage the first clinical trials were started in Salisbury in August, 1947 (Blair et al. 1947). The results after three weeks' treatment at this dosage were disappointing. Eight weeks after treatment only 9 of 40 patients with *Schistosoma hæmatobium* infections and 2 of 11 with *S. mansoni* infections had ceased to pass eggs. In this series and at the doses given (up to 4 mg. per kg. of body-weight daily for 15–21 days) the therapeutic effect was not great enough to be of real clinical value.

It was noted, however, that in this series some patients ceased to pass eggs for a short time soon after treatment; so trials were continued with small groups of patients at higher doses and on more concentrated courses. The full results of this work (Blair et al. 1949) showed that *S. hæmatobium* infections could be cured with larger doses of miracil D given for a shorter period, that on the whole the drug was well tolerated, and that no serious toxic signs appeared.

Halawani et al. (1948), describing clinical trials in Egypt, reported severe toxic reactions, miracil D being not well tolerated. They concluded that the effective dose was not less than 18–20 mg. per kg. daily for 7–8 days. Watson et al. (1948a), also working in Egypt, noted that the results with lower dosages were erratic, but that with bigger and more frequent doses the results were more consistent and the improvement greater. Most cases, however, later showed "partial relapse." Toxic symptoms were generally slight and affected only 1 in every 5 or 6 patients.

CLINICAL TRIALS

The present cases were treated with miracil D supplied by the Medical Research Council through Dr. Frank Hawking, to whom we are much indebted. Patients were chosen from African children of either sex attending the Salisbury African School, where a complete record of existing infections was kept. Urine and stool specimens were re-examined, and the trial group consisted of children with active *S. hæmatobium* infections. Some of these children also had *S. mansoni* infection evident in the stools. Each child was weighed, and an ideal dose schedule was calculated to the nearest 200 mg. on one or other of the following scales:

(1) 15 mg. per kg. daily for 5 days (total 75 mg. per kg.).
(2) 20 mg. per kg. „ „ „ „ (total 100 mg. per kg.).
(3) 25 mg. per kg. „ „ „ „ (total 125 mg. per kg.).

The early follow-up results on the lower dosages were so promising that the 25 mg. per kg. group was abandoned and, so far as possible alternate patients were given 15 or 20 mg. per kg. daily. The patients in each school class were treated as a group at the Salisbury African School from Mondays to Fridays inclusive. All treatment was given in the class-room by one of us (F. G. L.) and the tablets were swallowed in his presence. In most cases the full calculated dosage was given in ten equal doses to the nearest 200 mg. tablet. The morning dose was given at 8.15 A.M., and the afternoon dose at 4 P.M. No attempt was made to trace children to their homes if they were absent from school during treatment. Any patient who had not quite completed his course by Friday afternoon was encouraged to attend on Saturday morning for further treatment. When only a single dose had been missed, it was often possible to make the full dosage up within the five-day period.

The children weighed 60–155 lb. (27–70 kg.), and the total dosage in cured cases ranged from 2·0 to 7·6 g. A few children took only one or two doses, receiving less than 1 g. of miracil D, and of course continued to pass eggs.

The accompanying table shows the results of treatment checked by re-examination of specimens of stools and urine at intervals up to twelve weeks after the completion of treatment. Of 102 patients with *S. hæmatobium* infections, 53 took the "ideal" course in five days—15, 20, or 25 mg. per kg. daily. Of the remaining patients, 29 received what has been arbitrarily determined as a "satisfactory" course of treatment. These are patients who did not take the "ideal" course planned for them but received treatment for three to six days in excess of the following scale:

(1) If 3 days' treatment, more than 20 mg. per kg. daily
(2) „ 4 „ „ „ „ 15 mg. per kg. „
(3) „ 5 „ „ „ „ 12 mg. per kg. „
(4) „ 6 „ „ „ „ 10 mg. per kg. „

In other words, a total dosage of 60 mg. per kg. given in three to six days was classed as a "satisfactory" course. The remaining 20 patients took less than this quantity of miracil D, or had treatment for less than three days and are classed as "unsatisfactory." Some of these children took as much as 50–58 mg. per kg.,

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Treatment	Daily dose of miracil D for 5 days											
	15 mg./kg.				20 mg./kg.				25 mg./kg.			
	Cured	Dead eggs	Failed	Total	Cured	Dead eggs	Failed	Total	Cured	Dead eggs	Failed	Total
S. hæmatobium infections:												
Ideal	25	2	2	29	14	5	2	21	3	..	..	3
Satisfactory ..	7	..	2	9	14	3	1	18	1	..	1	2
Unsatisfactory	5	..	5	10	5	..	2	7	..	..	3	3
S. mansoni infections:												
Ideal	1	..	2	3	2	..	4	6	..	..	..	..
Satisfactory ..	..	..	1	1	..	..	2	2	..	..	..	..
Unsatisfactory	..	..	1	1	..	..	1	1	..	..	1	1

and it will be noted that half the "unsatisfactory" group appear to have been cured.

FOLLOW-UP

All patients were re-examined at intervals for twelve weeks after the end of treatment. It was impossible to arrange a weekly examination because of the intervention of school holidays, but each child was examined, on an average, seven times in the twelve weeks. Urine specimens were collected under strict supervision at the school, being obtained at the mid-morning break after the children had had some exercise. Bennie (1949), working in this laboratory, has shown that the best time for collecting urine specimens for examination is soon after the patient has taken sharp exercise.

Each sample was examined microscopically after centrifugation, and a note was made of the amount of red blood-cells and schistosome eggs seen. In addition, the urine was examined for active miracidia with the miracidia examination rack and by the technique described by Meeser et al. (1948). As a result of these examinations each case was classed in one of three categories: (1) "cured," those who ceased to pass any eggs whatsoever and in whose urine no active miracidia were seen; (2) "dead eggs," cases where at one or more of the examinations after a month eggs were seen but could not be hatched to show active miracidia; and (3) "failed," with eggs and active miracidia in all or most of the specimens examined.

It is interesting that all cases shown as "failed" were failures throughout the follow-up. No case found to be passing eggs and active miracidia a month after treatment showed any improvement thereafter. There therefore seems to be little point in continuing the follow-up for more than a month. If true relapses occur, the egg production must be delayed for at least as long as three months after the end of treatment.

The full significance of "dead" eggs in the urine is not clear, but they may indicate the slow and continued passage through the vesical mucosa of eggs which have been trapped and have died in the tissues long before. "Dead" eggs are probably passed into the urine in some cases for months after the satisfactory destruction of the schistosome worms.

Of 15 patients with *S. mansoni* eggs in their stools, 13 were passing *S. hæmatobium* eggs in their urine. All 13 were cured of their *S. hæmatobium* infections, but only 2 ceased to pass *S. mansoni* eggs. Of the 2 patients with *S. mansoni* infection, only 1 was cured, giving a total of 3 cures in 15 cases.

DISCUSSION

It has been shown that urinary schistosomiasis in African school-children can be cured with miracil D given for five days in twice daily doses and that this dosage causes no symptoms whatever in about half the children. The other children complained of abdominal pain, loss of appetite, nausea, and/or headache, and dizziness, and no doubt were sufficiently troubled to "play truant" and so evade treatment. None of the children were, however, ill enough to seek medical aid. All the symptoms noted were subjective and naturally difficult to assess, but it is worth noting that there were fewer complaints from children on 15 mg. per kg. than from the other groups.

Some of the senior boys and girls were up to average African adults in weight and took as much as 1·2 g. of miracil D daily without any trouble developing.

There seems to be no advantage in giving more than 15 mg. per kg. daily. If "dead eggs" are counted as cured cases, 27 out of 29 who took this dosage (total 75 mg. per kg. in five days) were cured, compared with 19 cures in 21 cases treated with 20 mg. per kg. (total 100 mg. per kg.). If the "ideal" and "satisfactory" treatment groups are put together, and if "dead eggs" are claimed as cures, 74 of 82 patients (90%) can be said to have been cured.

Of the patients who received "satisfactory" or "ideal" courses of treatment 8 did not respond to miracil D and continued to pass living eggs of *S. hæmatobium* in the urine. These patients passed the typical highly coloured orange-red urine seen when miracil D is taken, so presumably the drug was being absorbed from their gastro-intestinal tract and excreted in the urine. It is not known whether further courses of miracil D may eventually kill the worms and cure the infection. It has been suggested that some people may be unable to metabolise miracil D into a compound which kills the worms.

Miracil D appears to be able to cure 90% of urinary infections with *S. hæmatobium*, provided a total dosage of at least 60 mg. per kg., spread over three to six days, is taken. In *S. mansoni* cases the therapeutic result with the same dosage is poor. The number of cases of this infection treated in this clinical trial and in previous work in Southern Rhodesia is small, but the general impression gained is that *S. mansoni* is more resistant to miracil D than is *S. hæmatobium*. This is contrary to the opinions expressed by Watson et al. (1948a and b), who claim that miracil D is effective against both species. We had hoped to compare our results with theirs, but this was impossible because they seem to have used too large a number of dose régimes in small numbers of patients with conflicting results. For this and other reasons we do not regard their work as providing a satisfactory assessment of miracil D.

Miracil D may prove expensive—on African native standards—even when manufacture is on a large scale. At the present price, made in small quantities in the laboratory, the average case costs about 8*s*. to treat. It may therefore be necessary for economic and administrative reasons to be satisfied with a less perfect cure-rate from using smaller doses. The advantage of a drug which can be given by mouth, over other forms of treatment which have to be injected intravenously or intramuscularly is that mass treatment of urinary schistosomiasis can be applied in the village, with patients ambulant and without skilled staff or expensive equipment.

SUMMARY

Miracil D was given by mouth twice a day for three to six days to African school-children.

Of 82 children given a total dosage of at least 60 mg. per kg. of body-weight, 74 ceased to pass living eggs or

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active miracidia. None of these cured cases relapsed up to twelve weeks after treatment.

A few children infected with *S. mansoni* were treated with similar doses but the results were unsatisfactory.

We are grateful to Dr. R. M. Morris, Secretary for Health, for permission to submit this paper for publication.

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AN IN-VITRO TEST OF THE TOXIN-PRODUCING CAPACITY OF CORYNEBACTERIUM DIPHTHERIÆ

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IF an antigen and its precipitating or flocculating antibody diffuse towards each other in an indifferent gel—e.g., gelatin and agar—a sharply defined streak of precipitate appears under certain conditions.

A similar reaction is obtained if the antigen is allowed to diffuse in a gel containing a constant concentration of antibody, and vice versa. Reactions of this kind were described by Bechhold (1905) working chiefly with goat serum and anti-goat serum obtained from rabbits, and by Petrie (1932), Sia and Chung (1932), and Kirkbride and Cohen (1934), who described specific and non-specific halo reactions round colonies of meningococci, pneumococci, and shigellæ growing on media containing immune serum. Similar toxin-antitoxin reactions have since been described by Petrie and Steabben (1943), working with gas-gangrene bacteria, and by Ouchterlony (1948a) and Elek (1948) working with *Corynebacterium diphtheriæ*. I have also used the diffusion method in qualitative and quantitative analyses of antigen-antibody reactions (Ouchterlony 1948b and c). Other modifications of the diffusion technique for immunological analyses were earlier described by Oudin (1947).

The range of application of this method of studying antigen-antibody reactions may be briefly illustrated by the following examples. When a mixture of antigens X, Y, and Z diffuses in a gel towards an immune serum containing the corresponding antibodies *x*, *y*, and *z*, a precipitation "spectrum" is obtained containing several "lines" (fig. 1A). This phenomenon is undoubtedly connected with the establishment of narrow regions where antigen and corresponding antibody appear in the optimal proportions for the formation of a precipitate. The positions of the precipitates in relation to the diffusion centres therefore depend on such factors as initial concentrations of the participating reagents, their diffusion-rates, the time necessary for formation of visible precipitates, and the solubility of antigen-antibody complexes. By absorption of immune serum with appropriate antigens, or by removal or destruction of antigens in the mixture, the appearance of lines in the spectrum can be prevented selectively (fig. 1B and C).

If two different antigen preparations are allowed to diffuse towards the same serum (fig. 2), even small differences in antigenic composition can be detected. Identical precipitates fuse into a single streak, whereas unlike ones cross without evidence of interference. In fig. 2 three types of reactions are represented in which a mixture of three antigens may be present in each of the two antigenic samples. A shows the result of an experiment with two identical samples; the precipitates are V-shaped and symmetrical. B illustrates the case where one of the three antigens is present in different concentrations in the two samples; the corresponding precipitate appears asymmetrical. In the final example (C and D) one sample lacks one component, and here there is no interference. By this method it is possible to detect in commercial anti-diphtheria sera at least four different antibodies besides the antitoxin.

I describe here the technique of this in-vitro test of the toxin production of *C. diphtheriæ* and compare it with in-vivo tests.

MATERIAL

The material tested consisted of 2039 strains of *C. diphtheriæ*. Most of them were freshly isolated from throat and nose swabs sent to the diphtheria section of the State Bacteriological Laboratory, Stockholm, for routine examination. Clauberg-Herrmann's so-called indicator plates (dextrose and water blue) containing 0·08% potassium tellurite were used as a selective medium for the primary culture of the organisms. From this medium likely looking colonies were cultured on 10% sheep's blood agar. The diphtheria types were classified on the basis of the appearance of the colonies, hæmolysis, and their capacity of fermenting dextrose, sucrose, and starch. In dubious cases other media as well—e.g., McLeod's—were used for the classification of types. The distribution of the investigated material according to types was 5·5% gravis, 0·6% intermedius, and 93·9% mitis.

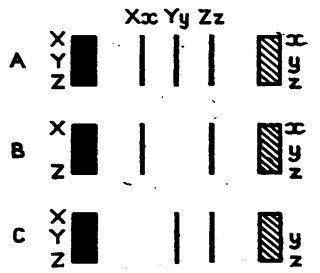

Fig. 1.—Precipitation "spectra" obtained when antigens diffuse in a gel towards immune serum containing corresponding antibodies: A, normal "spectrum"; B, C, "spectra" modified by alteration of conditions (see text); X, Y, Z, antigens; *x*, *y*, *z*, corresponding antibodies.

METHODS

In-vivo Tests.—The toxin-producing capacity of all strains was tested by subcutaneous inoculation into guineapigs. Tubes with 10% serum broth were seeded with pure cultures and incubated for 48 hours at 37°C in an oblique position. Of these cultures 1 ml. was next inoculated into guineapigs each weighing about 250 g., the observation period being 6–10 days. Necropsies were done on all dead animals, and toxic lesions in the suprarenal glands were noted.

In-vitro Tests.—To obviate any irregularity in the bottom of the petri dishes (10 cm. diam.) 1·5–2% of meat-infusion agar or water agar was poured on to form a thin layer. On top of this a surface layer of 1·5–1·75% meat-infusion agar mixed with 30–50% bovine or equine serum was added. Suitable quantities of diphtheria-immune serum were added to the surface layer in either of two different ways designated S and X.

In the S method different quantities of immune serum were added to the surface layer before pouring, so that a series of plates with different concentrations of antitoxin (40–0·63 FL.U. per ml. of medium) was obtained for each test. From four to six strains, as well as a known toxin-producing strain (Park William 8) as a control, were inoculated on each plate. The plates were incubated at 37°C and read after 48 and 96 hours. After one and two weeks longer at room temperature the plates were again examined. Halo reactions of toxin-antitoxin character round the colonies were reported as a positive reaction.

In the X method the surface layer consisted of plain serum agar. A strip of this was removed, and the trench was filled with serum agar to which a certain amount of immune serum had been added. The strains to be tested were inoculated in streaks at right angles across the trench. At least one streak

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of Park William 8 was included in each plate as a control. The plates were incubated at 37°C and read after 24, 48, 72, and 96 hours. By this method positive reactions appeared as thin beamlike precipitates extending from the streaks of bacteria.

RESULTS

The comparative results of primary in-vivo and in-vitro tests for all groups were as follows:

Guineapig		*Plate*		*No. of strains*	
+	..	+	..	1000	
+	..	−	..	45	
−	..	+	..	41	
					1086
−	..	−	..		953
			Total		2039

Of 2039 strains tested about half were toxic and half non-toxic. A lack of conformity between the in-vivo and in-vitro methods was observed in the primary tests on 86 occasions—i.e., in 4·2% of the total material. Positive animal tests and negative plate tests were registered in 2·2%, and the reverse in 2%. If only the in-vitro test had been used, 45 (4·1%) positive strains would have been missed—i.e., the in-vitro test was negative for these strains, whereas the in-vivo test was positive. This value will hereafter be called "percentage loss," and it amounted to 3·8% for the in-vivo method. The percentage loss in primary tests thus showed no significant difference between the in-vivo and in-vitro methods.

The results of a supplementary examination of the 86 strains which showed divergent results on the first examination of in-vivo and in-vitro tests were as follows (this control was made from original cultures of these same strains and with the same technique as in the primary testing, and the examination was repeated from one to three times until uniform results were obtained):

Primary results				*Positive strains*		
Guineapig		*Plate*		*Presumptive*		*Confirmed*
+	..	−	..	45	..	21
−	..	+	..	41	..	24

Of the 45 toxic strains in the first animal test 46·7% gave positive results in the further animal and plate tests. The remainder were non-toxic in both tests. Of the 41 primarily plate-positive strains 58·5% gave positive results in both animal and plate tests when the examination was repeated. The remainder gave negative results with both methods.

Since the in-vitro method seemed to give reliable results, different modifications were tried to get a convenient routine technique. These modifications of the plate method were used in different test groups, and the following observations were made.

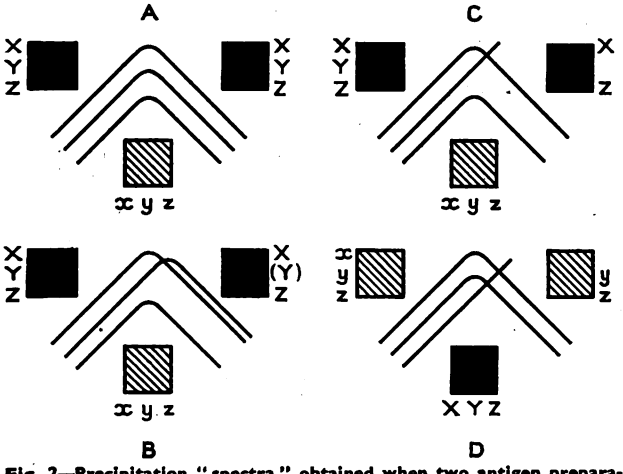

Fig. 2—Precipitation "spectra" obtained when two antigen preparations diffuse in a gel towards one preparation of antibodies or vice versa: A, both antigen preparations are identical; B, one of the antigens is present in different concentrations; C, D, one antigen is absent from one of the preparations; X, Y, Z, antigens; x, y, z, antibodies.

In the first group 237 strains were tested by the S method. Seven antitoxin concentrations were used. Of 133 primary positive strains the percentage loss was 9·1 with this technique, compared with 6 in the animal test. The highest antitoxin concentrations with which given strains reacted were as follows:

Highest concentration of antitoxin giving positive reaction

FL.U. per ml. of medium ..	12·5	10·0	7·5	5·0	2·5	1·3	0·6
Percentage of all strains ..	31·7	29·4	21·4	10·3	6·3	0·8	..

A single strain is included in only one antibody concentration.

In 92% of the toxic strains a positive reaction appeared within 48 hours, and in 8% in 96 hours. No further positive reactions were observed one and two weeks later. Calculated on the antitoxin concentrations 10, 5, 2·5, 1·3 FL.U. per ml. of medium, most of the strains showed a reaction in two or three consecutive serum concentrations. The range of reacting concentrations ("zone width") was limited to one in 13%, two in 65%, and three in 22%.

To find out the influence of potassium tellurite on the toxin-producing capacity of *C. diphtheriæ* the second group, consisting of 308 strains, was tested simultaneously by the S method with potassium tellurite (S.T.) and without (S). Five antitoxin concentrations were used (see below). The potassium tellurite was used in 0·16% concentration—i.e., twice the highest concentration used in ordinary diphtheria selective media. Of 202 primary positive strains the percentage loss was 2 with the S, and 3 with the S.T. technique, compared with 6·4 in the animal test. As regards the highest antitoxin concentration in which positive reactions were observed, there existed a positive correlation between the two media tested, but with a slight difference in favour of higher concentration for the medium without tellurite:

Highest concentration of antitoxin giving positive reaction

FL.U. per ml. of medium ..		40	20	10	5	2·5
Percentage of all strains	S	1·1	52·1	36·0	10·8	..
	S.T.	7·0	32·8	52·7	7·5	..

The zone width of the toxin reaction of the strains also corresponded in the two media, most of them showing reaction in two or more consecutive concentrations of antitoxin:

Zone width of positive reactions

Consecutive dilutions giving positive reactions ..		1	2	3	4
Percentage of strains	S	23·2	46·3	28·4	2·1
	S.T.	25·3	53·1	19·5	2·7

The time for appearance of positive reaction was also about the same. At 48 hours 83% of S and 81% of S.T. were positive; at 96 hours 17% of S and 19% of S.T. were positive. After 96 hours no further positive reactions were observed, even after another week.

In the third test group, containing 283 strains, a comparison was made between the S and the X methods. In the S plates the same content of antitoxin was used as in the second test group. In the X method a content of antitoxin equal to 90 FL.U. per ml. of medium ($=X_{90}$) was used in the trench. Of 188 primary positive strains the percentage loss for the S method was 1·1, and for the X_{90} 2·6, compared with 1·1 in the animal test. According to these results no significant difference between the S and X methods was observed.

Since the X method was found to be very convenient for routine work it was used as the only type of plate method in the fourth test group consisting of 400 strains. The percentage loss for X_{90} was 1·2 of 164 primary positive strains, compared with 3·0 in the animal test.

In the fifth group, containing 285 strains, double tests were performed with the X method at concentration X_{90}. The strains were tested primarily from the pure culture as in the previous groups (X_{90}), and again simultaneously with the guineapig test and with the identical serum-broth culture used for this in-vivo test ($X_{90}G$). On the primary investigation of 120 toxic

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strains the percentage loss was 3·3 with the X method, compared with 3·3 in the animal test. No difference between the results of X_{90} and $X_{90}G$ could be observed.

To investigate the presence and frequency of precipitations unrelated to diphtheria toxin—so-called false toxicity reactions—the X method was used with two different antitoxin concentrations in the trenches. These were 300 and 40 FL.U. per ml. of medium (X_{300}, X_{40}) and were tested in a sixth group, consisting of 310 strains. The true toxin reactions were identified by testing for interference with the toxin of Park William 8. This strain was inoculated at the same time alongside each strain to be tested. In 147 toxic strains the percentage loss was 13·6 for X_{300}, and 2·8 for X_{40}, compared to 5·5 for the animal test. The use of a higher content of antitoxin in the trench caused a number of precipitation reactions which were not of toxin-antitoxin character. For 320 strains tested X_{300} showed such false reactions in 46%. The corresponding value for X_{40} was 13% in 310 strains. With X_{300} such reactions were observed in both toxic and non-toxic strains. With X_{40}, however, they occurred only in non-toxic strains.

In the seventh test group, containing 216 strains, the X method was used with 40 FL.U. per ml. of medium. Of 134 primary positive strains the percentage loss was 9·0, compared to 0·7 in the animal test.

The time for appearance of positive reaction with the X method—X_{40} or X_{90}—was 48 hours in 92·3% of 712 toxic strains, and 96 hours in 7·7%. The corresponding figures for 399 toxic strains, where readings were made daily, were 24 hours 51·5%, 48 hours 39·3%, 72 hours 6·8%, and 96 hours 2·4%. With the X method it was thus possible to read more than half the positive reactions after a day, and a little more than nine-tenths of the reactions after two days. This demonstrates an agreement between the S and X methods.

As regards tests on guineapigs, the survival time of the animals in definitely positive toxin reactions has been surveyed. A total of 1045 diphtheria strains were found to be lethal to guineapigs: 54·2% caused death in 24 hours, 37·8% in 48 hours, 6·1% in 72 hours, and 1·8% in 96 hours. In 0·7% the animals survived for more than four and up to nine days.

Finally, the times required by individual strains to give positive results with the in-vivo and in-vitro methods were compared. The two-day cultivation in serum broth in the animal test is not included. The results were as follows:

	Time of positive reactions		
	Guineapig		
Plate	2 *days*	4 *days*	*Total*
2 days	594	63	657 (*92·2%*)
4 days	47	8	55 (*7·8%*)
Total ..	641 (*90%*)	71 (*10%*)	712

Of 712 strains examined by the X method and the guineapig test, 594 showed early reactions with both methods; 8 gave consistently late reactions; and 110 (15·4%) behaved irregularly. A similar agreement was found in a separate analysis of 369 toxic strains where a more detailed study was possible, readings having been made at 24-hour intervals. The percentage of these strains giving positive results within one, two, three, or four days was 51·5, 39·3, 6·8, and 2·4 respectively for the X method, and 45·8, 42·6, 9·2, and 2·4 respectively for the guineapig test.

DISCUSSION

The toxin-producing capacity, of 2039 diphtheria strains was tested, and positive results were obtained for 1086 strains in parallel in-vivo and in-vitro tests. The percentage loss in the animal tests was 3·8, and with the plate method 4·1, and no significant difference could be shown in the reliability of the two methods. Further, no such difference was noted in either of the seven investigation groups when various modifications of the plate method were examined. In these groups the percentage loss with the plate method was 1·2–9·1. The corresponding figures for the animal tests were 0·7–6·4. On continued examination of the strains which had given positive toxicity reactions with only one of the two methods in primary testing the toxicity was verified in about half the strains. This variation in results may be explained in different ways. Experimental errors must be expected in any method, of course. More important in this connexion, however, seems to be the variability of *C. diphtheriæ* in its capacity to produce toxin. Primarily toxic strains with a great tendency to dissociate into non-toxic variants often give negative toxicity results on repeated examination, since it is likely that only non-toxic bacteria are transferred in passages.

The two methods varied in the time required to show positive results; but the reaction time was practically the same, and strains reacting quickly in one method usually behaved similarly in the other. In view of the fact that in-vivo tests require two days' culture in a fluid medium, it is clear that the in-vitro technique saves about 48 hours and spares the use of animals.

As already mentioned, some modifications of the plate method were used. With the S method it was possible to make not only qualitative determinations of the toxin-producing capacity of the strains but also approximate quantitative estimation of the toxin production. Strongly toxin-producing strains give a positive reaction in higher concentrations of immune serum than do weakly toxin-producing strains.

The S method as a routine has the disadvantage that a comparatively large number of plates are required. In the above-mentioned test groups one or two plates were required for each strain tested, depending on the range of the plate series (5–7 concentrations and a control without immune serum). With the X method the number was considerably smaller, since 4–8 strains as well as the control were inoculated on the same plate. The X method also offers another advantage. The toxicity reactions may easily be verified by interference and crossing phenomena with a known toxin-producing strain. Further, it is easier to obtain suitable immune serum concentrations for toxin-antitoxin reactions with the X method than with the S method. With the X method immune serum diffuses at right angles to the toxin, and thus different concentrations are obtained in the same plate.

A satisfactory medium for testing the toxin-producing capacity of the strains by the plate method was ordinary meat-infusion agar with the addition of 30–50% equine or bovine serum. The addition of 0·16% potassium tellurite to the medium did not appreciably influence the reaction of the diphtheria strains tested.

SUMMARY

A toxin-antitoxin reaction in agar medium is presented as a routine toxicity test of *Corynebacterium diphtheriæ*.

In this plate method interference and crossing reactions with known toxin-producing strains make it possible to differentiate between true and false precipitin reactions.

The reliability of the in-vitro method is about the same as that of in-vivo tests on guineapigs.

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ESTIMATION OF p-AMINOSALICYLIC ACID IN BLOOD AND URINE

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THE increasing use of *p*-aminosalicylic acid in the treatment of tuberculosis has emphasised the need for quick and accurate methods for its assay in body fluids. Hitherto, the estimations have generally been done either by methods depending on the estimation of salicylates (Volterra and Jacobs 1947), or by the Ehrlich method and its recently described modification (Klyne and Newhouse 1948). The method of Volterra and Jacobs suffers from the disadvantage that, in our experience, the colour is not very satisfactory or easy to match, and allowance must be made for other salicylates present. The Ehrlich method is fundamentally a method of estimating primary aromatic amines, and hence is not suitable for use in the presence of sulphonamides or *p*-aminobenzoic acid; moreover, it will not estimate derivatives of N-acylated *p*-aminosalicylic acid.

In an attempt to obviate these difficulties we have developed a method of estimation based on the fact that *p*-aminosalicylic acid is a phenolic amine and will couple with diazotised amines to give a dyestuff. Sulphanilic acid has been found to be a convenient amine for this purpose, and, when this is diazotised with sodium nitrite and added to a solution of *p*-aminosalicylic acid in water, deproteinated blood-serum, or urine, a stable cherry-red colour is developed which is suitable for estimation by the usual colorimetric methods. It has been shown that, although the amino group in *p*-aminosalicylic acid is readily acetylated in the body, the hydroxyl group is not attacked, and the method should be applicable to both *p*-aminosalicylic acid and its N-conjugates. Salicylates might, on theoretical grounds, be expected to interfere with the estimation, but, in practice, they give a far less intense colour than *p*-aminosalicylic acid.

The excretion of *p*-aminosalicylic acid is so rapid that the concentration in the urine quickly reaches very high levels (*circa* 400 mg. per 100 ml. in 1 hour), and, for estimation at these concentrations, more rapid results can be obtained by making use of the characteristic salicylate colour obtained on the addition of ferric chloride.

Bray et al. (1948) have reported that *p*-aminosalicylic acid is excreted mainly unchanged or as the 4-acetamido compound, and it is noteworthy that 4-acetamidosalicylic acid also gives the characteristic purple-red ferric chloride coloration, and that the presence of this compound in the urine does not vitiate the estimation; the figure obtained can reasonably be taken as representing total *p*-aminosalicylic acid.

Preliminary results from these laboratories agree with the findings of Bray et al. and indicate that, when *p*-aminosalicylic acid is given by mouth as the sodium salt, the bulk of the material is excreted in 2–3 hours. With a single dose of 2 g. of the sodium salt, excretion in the urine is negligible after $3^1/_2$–$4^1/_2$ hours.

ESTIMATION OF p-AMINOSALICYLIC ACID IN BLOOD

The following method, involving the coupling of diazotised sulphanilic acid with an alkaline solution of *p*-aminosalicylic acid, has been found to give satisfactory results.

Diazo Solution.—Sulphanilic acid solution (1% sulphanilic acid in 10% hydrochloric acid) is cooled (0–5°C) in ice and 10% sodium nitrite solution added until the reaction is just positive to starch iodide; then a little of the sulphanilic acid solution is added until the starch-iodide test is negative. Free nitrous acid must be avoided, as this gives a coloration with blood-serum. This solution is kept cold (0–5°C) and made up fresh for each test. It is not recommended that it be used after standing longer than $^1/_2$ hour.

Method.—Blood-serum (2 ml.) containing *p*-aminosalicylic acid equivalent to 10–20 mg. per 100 ml., diluted with water (2 ml.), is deproteinated with 10% trichloracetic acid (2 ml.) and filtered. The clear water-white filtrate (2 ml.) is made strongly alkaline by the addition of 30% sodium hydroxide solution (0·25 ml.) and the diazo solution (0·25 ml.) added.

The colour is developed almost immediately and is compared with that obtained from standard aqueous solutions of *p*-aminosalicylic acid equivalent to 10–20 mg. per 100 ml.

Sulphonamides and *p*-aminobenzoic acid give no coloration in this test, and normal blood (i.e., containing no *p*-aminosalicylic acid) gives a negligible coloration. Salicylic acid gives a coloration which, for equivalent quantities, is only about 5% of that obtained with *p*-aminosalicylic acid. The recovery of added *p*-aminosalicylic acid from blood and blood-serum has been found to be 90–100%.

ESTIMATION OF p-AMINOSALICYLIC ACID IN URINE

This method (see Venkataraman et al. 1948) depends on the production of a stable colour when a solution of *p*-aminosalicylic acid, at pH 1–2, is treated with ferric chloride. Salicylic acid will, of course, interfere with this estimation, and if this method is to be used the patient must not have consumed aspirin or other salicylic-acid derivatives during the preceding 12 hours. When the patient is receiving salicylate therapy, the method described for the estimation in blood can be used, but large dilution of the urine may be necessary.

Method.—Calcium chloride solution (5–10 drops of 10% solution) is added to an aliquot (10 ml.) of the urine sample, the pH is brought to 8–9 with 3*N* ammonia, the solution is filtered, and the filtrate and washings are adjusted to pH 2 with 10% hydrochloric acid. The intensity of the colour developed on the addition of 2 drops of 10% ferric chloride solution is observed on a sample, and, if necessary, the urine is diluted to give a colour approximately equivalent to that obtained from a standard solution of *p*-aminosalicylic acid (i.e., 10 mg. per 100 ml.). The amount of *p*-aminosalicylic acid in the sample can be estimated colorimetrically with an accuracy of ± 5%.

With a heavy urinary excretion of *p*-aminosalicylic acid, where the sample has to be diluted to between 1 : 20 and 1 : 40, the preliminary treatment with calcium chloride is unnecessary and the estimation can be carried out directly on the diluted sample.

We would like to acknowledge the help we have received from the staff of the Pathological Department at the Royal Southern Hospital, Fazakerley, in particular Dr. C. A. St. Hill and Mr. R. E. Elliott.

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". . . The scope of psychiatry has increased beyond all imagination in the last century. Starting with kindly but essentially expectant treatment of the mentally ill in hospitals, it has gained knowledge of the nature of mental disorders and of the influence of the emotions upon the various physical complaints to which human flesh is heir. It has extended into the schools and into the factories; child psychiatry has become a specialty within itself; the private practice of psychiatry has increased enormously, indicating a readiness of persons who are suffering from emotional conflicts to seek advice rather than to attempt to battle out their problems alone and too often unsuccessfully. From being primarily interested in the institutional care of the psychotic, psychiatry has expanded to a study of the motives and the mechanisms of conduct of people in dealing with other people."—WINFRED OVERHOLSER, *J. Hist. Med.*, 1948, **3**, 381.

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Medical Societies

ASSOCIATION OF CLINICAL PATHOLOGISTS

London Meeting

THE 41st scientific meeting of this association was held at Westminster Hospital, London, on Jan. 27–29.

TUBERCULOSIS WITH AGRANULOCYTOSIS

In his presidential address Dr. F. B. SMITH (Kendal) described what appeared to be a new syndrome of atypical (septicæmic) tuberculosis with agranulocytosis. In 4 adult cases with pyrexia, purpura, and agranulocytosis, there was heavy blood-borne bacterial infection as evidenced by dense colonies of mycobacteria in the liver, spleen, and the few lymph-nodes found at necropsy; yet there was no typical histology of tuberculosis and no clear primary focus.

OVARIAN TUMOURS

Dr. C. W. TAYLOR (Birmingham) described the various virilising tumours of the ovary. These, he said, fell into two groups: (1) arrhenoblastoma with structures of testicular type (differentiated or embryonic), and (2) lipoid-cell tumours of the so-called adrenal-like type. He showed how in each of his cases removal of the tumour resulted in regression of masculinisation and return to a normal menstrual cycle in one month; in 2 cases full-term pregnancy followed, with lactation. He thought it unwise to accept the virilising lipoid-cell tumour as of heterotopic adrenal origin.

FAT EMBOLISM

Dr. H. R. R. MAVOR (Lincoln) described the changes in fat embolism of the brain with large numbers of intravascular fat plugs. It was possible to detect two types of hæmorrhage, minute foci of necrosis, and focal degeneration, involving the neurons, the axons, and eventually the myelin sheaths—with glial infiltration of the lesions if the patient survived long enough.

BACTERIAL FLORA IN GASTRO-ENTERITIS

Dr. CHRISTOPHER GILES (Stoke-on-Trent) described an investigation into the coliform flora in gastro-enteritis. The H type of *Bacterium coli* was isolated from 94·7% of the fæces of 207 cases of gastro-enteritis, whereas it was found in only 1·8% of 721 controls; antibody titres were found in 60% of 41 cases and in only 1·2% of controls. In 55 necropsies the organism was found almost constantly in the gastro-intestinal tract and sometimes in the mesenteric lymph-nodes, the liver, and the spleen. Feeding experiments were unsuccessful except with 10 newborn guineapigs, of which 5 developed diarrhœa and 3 died, with necropsy findings similar to those in infants. Dr. JOAN TAYLOR, who had also found such a strain (called by her D433) in sporadic outbreaks of gastro-enteritis, was still sceptical about its pathogenicity.

EPIDERMAL TUMOURS

Dr. GEORGIANA BONSOR (Leeds) gave an account of 57 melanin-forming epidermal tumours observed in collaboration with Prof. M. J. Stewart. These tumours were classified histologically as squamous papillomas (21), benign calcified epitheliomas (2), basal-cell cancers (28), and squamous cancers (6). Distinct from the true benign and malignant melanomata, which are of neurogenic origin, they tended to affect patients over 50 years of age, and to occur more commonly on the face and neck than on the trunk and extremities; they did not metastasise, and the history was usually long. They were no more malignant than their non-melanin-forming counterparts, and they responded to the same type of treatment.

HÆMATOLOGY

Dr. J. HOOGSTRATEN (Cambridge) compared the in-vitro growth of leukæmic cells in serum of a healthy person with that in serum of the leukæmic patient. Immature leukæmic cells, although incapable of differentiation in vivo, would differentiate or mature in vitro when grown in normal human or animal plasma. Transfusions of fresh blood or plasma might produce temporary hæmatological and clinical improvement and even diminution in size of enlarged lymph-nodes and spleen; yet reconstituted dried plasma did not have this effect. In leukæmic cells cultured experimentally, the immature myeloblasts and myelocytes were found capable of a degree of differentiation in vitro resembling that of normal leucopoietic cells, with the same rate of proliferation and extent of differentiation whether grown in leukæmic or in normal serum. Normal plasma therefore did not exert its influence directly on leukæmic cells but possibly through an intermediary mechanism or another tissue.

Dr. M. C. G. ISRAËLS (Manchester) made a strong plea for agreement in nomenclature of blood and marrow cells. There was already a measure of agreement in terminology of the white-cell series, but the position with regard to the red-cell series had been further set back by the proposals of the American committee, who wished to include such hybrid terms as "rubriblast," "rubricyte," and "metarubricyte," and who sought to call the megaloblast "pernicious-anæmia-type rubricyte." Subsequent speakers agreed that the terms now in use in this country were acceptable, and that what was really required, to avoid confusion, was a standardised description of the cells called proerythroblasts, megaloblasts, and normoblasts.

It was announced that the association had formed a committee on hæmatology.

Dr. J. MURRAY, Dr. E. N. ALLOTT, and Dr. C. A. HOLMAN described their routine investigation of fœtal hæmolytic disease with special reference to prevention and treatment—including the technique of replacement transfusion. Sir LEONARD PARSONS, F.R.S. (Birmingham) congratulated the speakers on their results which were second only to those published by Diamond in the U.S.A. He showed how in the best hands mortality had dropped from 50% almost to 10%. Dr. W. WEINER (Birmingham) described cases of leukæmia in which he had used replacement transfusion; he had produced some clinical improvement, which was, however, only temporary. Subsequent speakers doubted the wisdom of transfusion in leukæmia, especially in children where the agony of the parents had to be faced twice if there were a short remission following transfusion.

Dr. MARTIN HYNES (Cambridge) described his investigation of the iron reserves of normal man by bleeding until the rate of hæmoglobin regeneration reached a constant level. The daily absorption of iron from the food, in excess of the normal requirements to replace effete red cells, was calculated by the different rates of hæmoglobin regeneration when 6·5 ml. and 20 ml. of blood respectively were withdrawn daily after exhaustion of the iron reserves. The amount was estimated to be about 600 mg. The present English diet yielded only 4 mg. of iron daily for hæmoglobin synthesis; this would replace a loss of only 8 ml. of blood daily.

STEROID CHEMISTRY

Prof. E. C. DODDS, F.R.S., described the three 6-membered rings joined in phenanthrene configuration, with a 5-membered ring attracted to one of them, which gave the cyclo-penteno-phenanthrene nucleus; this was the basis of all steroid nomenclature. He also recalled that the hydroxyl groups were shown by the letters "ol" preceded by the number of the carbon atom to which the group was attached, whereas a ketone group was shown by the letters "one." He classified steroidal substances as (1) cholesterol, (2) bile acids, (3) œstrogenic substances, (4) progestational substances, (5) androgenic substances, (6) adrenocortical substances, and (7) steroidal substances of unknown origin. He mentioned the claims of Dobriner and his colleagues that many diseases were associated with a characteristic steroid pattern of excretion. Reference was also made to the claim that the presence of a particular steroid—Δ^9 etrocholenoline—was associated with malignant disease. He said that the main use of analysis of steroids isolated from the urine should be to differentiate between virilism of adrenal and of other origins.

Other subjects considered included deaths under anæsthesia.

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Reviews of Books

Modern Trends in Dermatology

Editor: R. M. B. MACKENNA, M.A., M.D. Camb., F.R.C.P., physician in charge, dermatological department, St. Bartholomew's Hospital, London. London: Butterworth. 1948. Pp. 431. 42*s*.

THIS is indeed a brave title; for in medicine some apparently modern ideas turn out to be old-fashioned, while others are rejected after a terrifyingly short vogue. Few will quarrel with the topics selected by Dr. MacKenna for inclusion in his first series, nor with the authorities chosen to deal with them. In a work containing so many fresh ideas and so much controversial matter it is natural for the reader to find notions with which he disagrees. Moreover, some of the writers approach the same subjects from different aspects, and arrive at dissimilar conclusions: thus Dr. Barber links the so-called seborrhœic group of disorders with malfunction of the sex-glands, whereas Dr. Wittkower uncompromisingly regards them as psychosomatic. Both are probably partly correct; and their contributions are the more thought-provoking in consequence. In medicine some of us are apt to cling to the traditional viewpoint overlong, and to resent the intrusion of new and unfamiliar ideas. The busy dermatologist will be grateful to Dr. MacKenna for this series of essays presenting new material in assimilable form. To those of an academic turn of mind Dr. Parkes Weber's masterly section on the necrobioses, atrophies, and scleroses, and his fine attempt at a classification of this difficult group of maladies, will appeal greatly. Though this is essentially a work for specialists and postgraduate dermatologists, there is much to interest the general reader.

Szondi-Test

Experimentelle Triebdiagnostik, Tiefenpsychologische Diagnostik im Dienste der Psychotherapie, Kriminal- und Berufs-psychologie, Charakterologie und Pädagogik. Dr. Med. L. SZONDI. Berne: Huber. 1948. Pp. 308 (and box of cards). Sw. fr. 68.

Dr. Szondi, a Hungarian psychologist, has devised an ingenious test of personality which, like certain other such tests, suggests to some a parlour game and to others the revival of an exploded theory of personality. The theory to which Szondi's test at first might be suspected of harking back is that of the physiognomists of the Lavater school and of typologists like Lombroso. The theory, however, propounded in the first volume makes no reference to these outmoded views, but concerns itself with a composite genetic-instinctual structure of human character to which the test allegedly serves as a diagnostic index.

The test consists in six sets of portraits: in each set there are eight faces—of a proved homosexual, a sadist, an epileptic, a hysteric, a catatonic schizophrenic, a paranoid schizophrenic, a depressive, and a manic person. These faces are mostly taken from the 1901 edition of Weygandt's textbook of psychiatry; the remainder are from other psychiatric books published between 1892 and 1922, together with ten more or less contemporary Swedish and Hungarian murderers, epileptics, and homosexuals. They make up, as may be imagined, a somewhat repellant assemblage. The subject of the test is shown each set of faces in turn, and asked to pick out the two he likes best and the two he finds most antipathetic. As the former task is, for many people, a difficult assignment, the subject may in such cases instead pick out the two faces he finds least disagreeable (*unsympathisch*). There are other subsidiary choices to be made, on the same lines, and the whole process is repeated within a few days or weeks, and then again until it has been performed ten times. The pictures he has picked out are then shown one by one to the subject, who is asked to give his associations to them and to say what he thinks might be the life-story of the person whose face is depicted. From his choices a profile and formula are derived which enable his basic character to be diagnosed, in terms of instinctual drives. The result can be applied to clinical diagnosis, criminology, vocational guidance, prediction of possible character changes, assessment of the effects of treatment upon his mental state, and the detection of latent tendencies in the carrier of morbid hereditary traits.

These are wide claims, and much more evidence will be required than that given here before they can all be accepted. But the test has been widely used and experience has shown that it can by no means be rejected on a-priori grounds; nor is it necessary to accept the curiously animistic mixture of unorthodox genetics and unorthodox psychology which the author puts forward, with detail and neologisms, to recognise in his method a useful addition to the procedures (including the Rorschach and the thematic apperception test) which indicate ways of enlarging our knowledge of personality. As Professor Thurstone has recently pointed out, these procedures, however unsatisfactory in their present state, demand and deserve study by sound psychological methods, including statistical verification.

Mesmerism

By Dr. MESMER. 1779. Being the first translation of Mesmer's historic "Mémoire sur la découverte du magnétisme animal" to appear in English. With an introductory monograph by GILBERT FRANKAU. London: Macdonald. 1948. Pp. 63. 6*s*.

Mesmer's place in the history of psychological medicine is assured, because he elaborated and made notorious a method of treatment out of which hypnotism grew: but it is still doubtful how far his contemporaries were right in attributing to him something of the charlatan. His conviction that a universal rarefied fluid acting upon the nerves produced the phenomena of "animal magnetism" was no doubt sincerely held, but his methods of applying it therapeutically were flamboyant and his flair for publicity excessive. The memoir in which he described his discovery and some of his cures had never been translated into English: Mr. Gilbert Frankau has rendered a service in getting this done and in writing an introductory note which gives a rapid and lively aperçu of the chequered history of mesmerism, though his enthusiasm leads him to make some undue claims for its founder.

Abdominal Operations

(2nd ed.) RODNEY MAINGOT, F.R.C.S., surgeon to the Royal Free Hospital, London. London: H. K. Lewis. 1948. Pp. 1274. 84*s*.

THE second edition of Mr. Rodney Maingot's outstanding work bears evidence of thorough revision. Authorities in special subjects have now been called upon to deal with new aspects of surgery and new operations, yet the whole remains consistent. As an account of present-day abdominal procedure it stands unsurpassed, a worthy successor to Moynihan's book which so long reigned supreme. Not all surgeons will unreservedly agree with all Mr. Maingot's statements, but he rarely makes assertions without responsible backing. He provides a reliable guide for the young and a reference book for the experienced.

Obstetrics and Gynæcology

A Synoptic Guide to Treatment. BEATRICE M. WILLMOTT DOBBIE, M.A., M.B., F.R.C.S., D.M.R.E., surgeon, Birmingham and Midland Hospital for Women. London: H. K. Lewis. 1948. Pp. 348. 20*s*.

HERE is a practical book, which wastes no time on theory but gets smartly down to business. About two-thirds of it is devoted to obstetrics and the remainder to gynæcology, and it is in the former section that most of the flashes of brilliance are to be found. The author's style is vigorous and lively, and anyone familiar with some of the difficulties she describes will recognise that her advice is as sound as it is downright and clear. In brief, she favours umbrella-hoisting before the cloudburst, and she backs her arguments with results from the Birmingham Maternity Hospital, a source with which nobody will quarrel. The section on gynæcology is not quite up to the same standard, but there is plenty of useful information in it. This book is worth having, not only for what it has to teach but also for the pleasure of reading it.

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Reticulosis and Reticulosarcomatosis

A Clinical and Pathological Study. Dr. P. VAN DER MEER, medical clinic of the University Hospital, Leyden; Dr. J. ZELDENRUST, pathological laboratory of the university. Leyden: J. J. Groen and Sons. 1948. Pp. 83. Fl. 4.90.

THE authors describe a detailed study of 18 cases of reticulosis and reticulosarcomatosis seen in their own practice. They have collected in convenient form much scattered information about these conditions and they discuss the question whether they are infective or neoplastic. Of their 7 cases of generalised reticuloses 6 were fatal, and the necropsy reports showed wide variety, though all had proliferation of the reticulum cells. The 11 reticulosarcomas mostly appeared first in a defined site, such as the nasopharynx or a group of lymph-glands, but afterwards there were multiple lesions very like those found in the reticuloses. X-ray therapy used in several of the cases gave good immediate results; but, except in one patient, the disease continued unchecked at other sites. Some interesting illustrations accompany the records, including photographs of reticulum cells in circulating blood and in marrow.

The Battle of the Conscience

EDMUND BERGLER, M.D. Washington: Washington Institute of Medicine. 1948. Pp. 296. $3.75.

THE exact differences between the conscience and the "superego" of the psycho-analysts has puzzled many an honest inquirer. Dr. Bergler expounds and dissects it in this book. He is not satisfied with the current psycho-analytic view that the superego, *tout court*, is the unconscious part of the conscience. He believes that in the superego there are two warring elements, expressing Freud's conception of the antagonism between life-instinct and death-instinct: one of these elements is the ego-ideal, the other is the destructive daimonion which "uses the Ego-Ideal for a silent model, constantly holding it to the frightened Ego with the eternal rebuke 'Have you fulfilled your self-created Ego-Ideal demands?' Every discrepancy between Ego and Ego-Ideal results in feeling of inner guilt." The book (which is largely built up from previously published articles) is devoted to intricate and at times contorted explanations of the ways in which guilt can be generated, and the part played therein by the conscience. Only a psycho-analyst—and not even all psycho-analysts—could follow Dr. Bergler through this maze, in which the hopeful traveller sees nothing directly, but through mirrors, prisms, and dissolving views.

Atlas of Human Anatomy

Vol. I. M. W. WOERDEMANN, M.D., F.R.N.A.SC., professor of anatomy and embryology, University of Amsterdam. Amsterdam: Wetenschappelijke Uitgeverij. London: H. K. Lewis. 1948. Pp. 440. 70*s*.

Professor Woerdemann is producing his atlas for students primarily in an attempt to combat the increasing scarcity of anatomical material for dissection. This volume, the first of three, deals with the locomotor apparatus and has three sections—osteology, arthrology, and myology. The last section is partly diagrammatic, but most of the figures in the atlas are drawn from actual specimens and dissections. The book has no text, but the 665 drawings are liberally annotated. The latinised B.N.A. terminology is used; and this, though it favours international use, is cumbersome in places (e.g., "vagina tendinum musculorum extensoris digitorum communis et extensoris indicis proprii"). All the figures are notable for their original approach and clearness, though several are too flat and a few show slight errors in proportion with crowding of structures. There is considerable accuracy of detail, with a few minor exceptions (in one figure the "twelfth" lumbar vertebra is shown articulating with the sacrum and in another diagram the origin of sternothyroid is shown to be above that of sternohyoid). Professor Woerdemann and his department are to be congratulated on the graphic presentation and individuality of this first volume. The second and third will deal with splanchnology and the cardiovascular and nervous systems.

Encyclopedia of Medical Sources (London: Baillière, Tindall, and Cox. 1948. Pp. 476. 41*s*.).—In publishing this dictionary of eponymic medical nomenclature, Dr. Emerson Crosby Kelly has met a need which many have experienced. An alphabetical list of surnames is followed by a subject index referring the reader to the required surnames. The omissions, however, are fairly numerous, and it is to be hoped that a future edition will include old favourites such as Kupffer's cells, Naboth's follicles, Petit's triangle, the cave of Retzius, Tenon's capsule, and Wormian bones.

There's No Need to Shout (London: Gollancz. 1949. Pp. 152. 8*s*. 6*d*.).—In this spirited autobiography Miss Frances Warfield tells what it is like to grow up hard of hearing and refusing to admit it. Her shifts, as she tells them, are funny, but they can hardly have been funny to get through. She learned to fake absentmindedness to get people to repeat what they had said; she learned to play the gramophone to get them to speak up; she learned to trick them into belief in her good hearing by her good jokes. On the last page she consents to wear a hearing-aid, with splendid results, and to the reader's great relief. An entertaining and disturbing little book.

The "Aids" Series (London: Baillière, Tindall, and Cox, 1948).—These little books, ranging from 5*s*. to 7*s*. 6*d*. in price, are well known to students revising before examinations. Fitting easily into the pocket, and carrying, for the most part, a great deal of essential information well packed down, they serve this purpose well. Since they are written by different authors, some are naturally better than others. Three which have just been issued—a second edition of *Aids to Physical Chemistry*, a third edition of *Aids to Psychology*, and a fourth edition of *Aids to Biochemistry*—are sound handbooks, though psychology, on which volumes might be (and have been) written, appears almost in the form of headlines, getting some 50 pages less than biochemistry and looking famished beside physical chemistry, which is more than double the size.

A History of Science and its Relations with Philosophy and Religion (4th ed. London: Cambridge University Press. 1948. Pp. 527. 25*s*.).—Sir William Dampier, F.R.S., deals here with every department of science, and is never dull. The description of developments in medicine is sound, and, since he approaches such things as penicillin and the sulphonamide drugs as a chemist rather than a clinician, he supplies the kind of facts liable to be missing from medical textbooks. The book allows the reader to view science as a whole, not as a set of isolated subjects, and it also helps him to see it in relation to other branches of learning. In an age suffering from the restrictions of specialism, such a synthesis is needed. Doctors who have no leisure for reading philosophy will find that Sir William writes as clearly of this subject as he does of science. His use of Whitehead's "philosophy of organism" in relating science to philosophy and religion is particularly apt.

Bone Marrow Biopsy (1st English ed. London. J. & A. Churchill. 1949. Pp. 433. 42*s*.).—Three years ago, in reviewing the original edition of this book by Dr. S. J. Leitner, of Berne, we noted that it was minutely detailed but uncritical, with chiefly Continental references. These characteristics unfortunately remain. An attempt has been made by Dr. C. J. C. Britton and Dr. E. Neumark, the revisers, to include English and American work, but the revision is patchy and much significant recent information is not mentioned. The illustrations, mainly photographs, often fail where clarity is most necessary—for instance, in the reproductions of megaloblasts. The colour plates, too, are disappointing, and have not been revised. Long tables of marrow counts in conditions like nephritis and tuberculosis have been retained. In the Swiss edition the titles of the papers quoted were given; in the English edition these have been omitted, and the reader is faced with pages of references (there are about 1000 to chapter VII alone) with no indication about content. Nor is it always possible to judge the value of these references from the text. Dr. Leitner's book certainly tells what is the Continental view of the effect of any given disease on any particular bone-marrow cell and on the marrow pattern as a whole. But the limited class of inquirer who needs this information would usually be capable of reading the Swiss edition.

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THE LANCET

LONDON: SATURDAY, FEB. 26, 1949

Management of Chronic Peptic Ulcer

I cannot eat but little meat
My stomach is not good.—*Old song.*

THERE is a growing body of opinion which believes that the regimen usually laid down for ulcer patients is too rigid. As with most diseases, the best chance of curing a peptic ulcer lies in diagnosing it early and treating it radically at once, however tempting it is just to stave off the symptoms when they are not incapacitating. But it is a melancholy fact that many ulcers cannot be permanently cured by medical treatment, and when surgery is contra-indicated, is refused, or has been tried in vain, the best that many patients can hope for is to lead reasonably normal lives with only occasional minor relapses. In these chronic cases, which still form a large proportion of the total, our task should be to help our patient to come to terms with his disability, avoiding restrictions based on tradition rather than evidence, and interfering as little as possible with his normal activities. During an acute relapse rest in bed is essential, but it must not be prolonged to the point of producing irritable boredom, or the aim of mental rest (which is probably even more important than physical rest) will be defeated. Later, when the patient returns to work, he should be allowed reasonable latitude. It is unreasonable to expect a restless, eager, and ambitious man, such as many ulcer patients are, to lead a frustrated vegetable existence. The brake must be applied, but gently and with a nice judgment of the individual.

The need for drastic food restrictions is open to question. Too strict dieting may lead to undernutrition and increase the liability to relapse, besides producing faddism and preoccupation with the processes of digestion. Furthermore, present-day rationing and the shortage of alternative foods make a strict diet both difficult and monotonous. Obvious gastric irritants such as spices, seasonings, peels, and pips are best avoided, but with these exceptions the patient should be allowed to eat anything which does not persistently disagree with him. Much more important than the composition of the diet is the regularity and timing of meals. Little and often should be the invariable rule, and the patient must plan his life so that meal-times are regular and unhurried. Wise employers who allow their dyspeptic employees time off for snacks between meals will thereby avoid the loss of their services through illness; and many ulcer sufferers are valuable skilled workers. The question of smoking will probably never be settled to everyone's satisfaction. No convincing experimental evidence has yet been brought forward to prove that it is harmful. SCHNEDORF and IVY,[1] for example, found that smoking did not increase gastric acidity; if it had any effect at all, it depressed gastric secretion and retarded evacuation. Both of these actions might be expected to be beneficial rather than harmful. On the other hand, many patients spontaneously cut down their smoking because they find it causes pain. But whether we regard smoking as a harmless habit, as a deplorable tic, or as a shameful addiction, we must face the fact that many people find it soothing to their nerves and cannot give it up without inducing irritability and restlessness. For these, to quote the "Disabilities" article of Feb. 12 (p. 279) "there is more disadvantage in discontented deprivation than in indulgence," provided the indulgence is not excessive. Once again, reasonable moderation is advisable.

The barbiturates are the only drugs whose value at all stages of peptic ulcer is indisputable. Belladonna, best given in the form of *lævo*-hyoscyamine, is useful in the acute stage, for it allays spasm and reduces painful gastric contractions. But there seems little point in continuing it once this stage is passed. As a routine antacids have little to recommend them. DOUTHWAITE[2] contends that it is impossible effectively to neutralise gastric acidity by means of antacids; this can only be done by continuous nasal drip-feeding with milk. Certainly ulcer pain is relieved more effectively by a light feed than by an antacid. Persistent pain which is not thus relieved requires rest in bed. However, if adherence to tradition demands that an antacid be given, magnesium trisilicate or colloidal aluminium hydroxide have the advantage of not producing alkalosis. There are drugs which are positively harmful to the ulcer patient. The danger of insoluble aspirin is now well known; hæmatemesis may result from its use. The soluble preparations seem less open to objection, but not every patient will remember to draw the distinction, and it is possible that even these increase the likelihood of bleeding[3]; so perhaps it is better to forbid salicylates altogether. Intercurrent pain which does not respond to phenacetin can safely be treated with the newer synthetic analgesics, which seem to be relatively free from irritative action on the stomach.

The successful management of a peptic ulcer, then, requires on the patient's part an avoidance of excess, a minimum of fuss, and an acceptance of the inevitable. It asks of the physician a humble recognition of the limitations of therapy and a sparing and humane use of his veto.

Topectomy

EGAS MONIZ, of Lisbon, has lately restated[4] the reasons which led him in 1935 to undertake prefrontal leucotomy. Where, as in melancholia and obsessional illness, the patient's thought and life is ruled by a dominant idea, the fault, he thinks, lies in abnormally fixed synaptic connexions between certain neurons; and he concluded that if these connexions could be severed the morbid constellations of ideas would be dispelled. He suspected the silent prefrontal areas of being the seat of the faulty synapses, and accordingly

1. Schnedorf, J. G., Ivy, A. C. *J. Amer. med. Ass.* 1939, **112**, 898.
2. Douthwaite, A. H. *Brit. med. J.* 1947, **ii**, 43.
3. See annotation, *Lancet*, 1943, **ii**, 419.
4. Moniz, E. *Disch. med. Wschr.* 1948, **73**, 561.

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attacked the white matter of these areas by surgery. He can hardly have expected that his *operatoires tentatives* would be taken up with such enthusiasm and used in treatment so widely as they are today.

With few exceptions neurosurgeons have followed MONIZ's practice of approaching the frontal lobes through small burr-holes. The cuts thus made vary in depth and plane, and many psychiatrists, observing wide differences in the results, would greatly prefer an open, precisely localised, operation. In 1946 a group of workers from Columbia University and the New Jersey State Hospital set out to determine the effects of bilateral ablation of different areas of frontal cortex, and we now have a short report by HEATH and POOL [5] on results in two series of cases in which Brodmann's map was used for orientation. The first series consisted of 24 chronic psychotic patients who had failed to respond to other forms of physical treatment; as controls 24 similar patients had the same preoperative "work-up" and were anæsthetised without operation. Nearly eight months later, 11 of those operated on were out of hospital (10 working at pre-illness capacity) but only 2 of the controls had improved sufficiently for discharge. In all patients showing improvement after topectomy, one or both of Brodmann's areas 9 and 10 had been removed, and undesirable sequelæ were noted only where ablation was more extensive than the sum of areas 9 and 10. In a second series of 15 private patients—most of them chronic psychotics who had been in hospital for many years—operation was confined to the region of these two areas: of these 15, 10 are working at full capacity and an additional 3 can live outside hospital under supervision. Complications have been few and there have been no deaths. The operation now preferred consists in removal of the posterior part of area 10 and the anterior part of area 9, but full details of the operative technique are not given. Where the specific site has been accurately removed, postoperative convulsions and incontinence have been absent; and even with ablation of other sites they are said to have been transient. The change in behaviour following ablation of areas 9 and 10 was in the sphere of affective response: emotions did not influence the patient so profoundly, and were more readily and appropriately discharged, without being noticeably blunted. Good results are therefore more probable where the illness has a strong emotional component and where this is congruous with ideation—e.g., in agitated melancholia, involutional paranoid psychosis, and the depressive phase of manic-depressive psychosis. Where mood and thought content are incongruous results are doubtful, and this must be taken into account when considering topectomy for mania and, in many cases, for schizophrenia. On clinical and psychometric evaluation of their cases, HEATH and POOL claim that after topectomy over-all intellectual function improves and there is no loss in the capacity for abstract thinking: when overt psychotic symptoms are removed, the personality is, they believe, essentially the same as it was before illness began.

The series of cases treated in this way is small, and the period of observation after operation is brief. Apparent improvement, followed by relapse, is not uncommon after leucotomy. Even so, to have 20 out of 39 patients working at full capacity a few months after operation seems a remarkable achievement, especially when one recalls that in the earlier cases differing areas were removed, and the final site of operation was chosen only after initial effects had been studied. All operations of this group remain at present empirical, and can be judged only by their results. But, other things being equal, it is best that they should be precise.

5. Heath, R. G., Pool, J. L. *Psychosom. Med.* 1948, **10**, 254.

Pale Epithelium in Mammary Tissue

ONE of the most obvious and striking histological features to be seen in sections of cystic breast material is the glandular tissue lined by large pale eosinophil epithelium. These glandular structures, when small, are grouped and apparently derived from acini; and indeed they may form part of a normal mammary lobule, though they are always larger than ordinary acini. Cellular hyperplasia and progressive dilatation of these structures leads to the formation of confluent cysts by rupture of intervening walls, and the end-stage of the process may be the cysts of various sizes, usually multiple but occasionally single, characteristic of "cystic disease" or "chronic cystic mastitis." If large and discrete, the cysts are often described as blue-dome in type.

The derivation and significance of this pale epithelium and of the cysts it forms have been the subject of numerous studies. Two main views have prevailed with regard to the origin of these pale structures: they represent actual or altered sweat glands or they are derived from ordinary mammary tissue. On the former view, pale epithelium represents sweat-gland tissue, normally or accidentally included in the breast substance, or indicates incomplete mammary differentiation from, or a metaplastic change to, an earlier sweat-gland cell type. A more elaborate argument is supported by HIGGINSON and MCDONALD,[1] in "an attempt to establish the status of the so-called pale epithelium of the breast." Their argument is based on the acceptance of SCHIEFFERDECKER'S [2] classification of cutaneous glands, which separates the ordinary "small sweat gland" of eccrine type from the "large sweat gland" and the mammary gland, both of which are included in the apocrine group. This postulates an identity of origin for the apocrine group based on the normal presence of pale epithelium, which thus represents the primitive gland from which the various members of the apocrine type are derived. Their argument is involved, and proof, as they admit, is inconclusive, though the view holds interest from a wider biological standpoint. All such theories, however, need critical examination, for they often raise more problems than they solve. Embryological studies of human tissue suggest that all the cutaneous glands, including the mammary gland, are derived independently from the primitive surface epithelium, and LUSTIG,[3] in a detailed study of embryos from an early stage, could find no sweat glands in or near the primary breast area. The combination of glandular elements, mammary and sweat gland of either type, would therefore be difficult to prove at any later stage of development.

1. Higginson, J. F., McDonald, J. R. *Surg. Gynec. Obstet.* 1949, **88**, 1.
2. Schiefferdecker, P. *Zoologica*, 1922, **27**, 1.
3. Lustig, H. *Arch. mikr. Anat.* 1915–16, **87**, 38.

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The attempt to answer any difficult pathological problem by evoking analogies and resemblances to an earlier stage of mammalian evolution is, in general, to be deprecated. It has a faint flavour, reminiscent of much modern autobiography, of explaining the "difficult" adult against the background of a maladjusted unhappy childhood. Arrested development, or an accidental heterotopia, provides an acceptable explanation for many pathological conditions, especially in young subjects; but similar assumptions regarding pale epithelium in the breast, based on staining reactions and morphological resemblances, are unconvincing. There is indeed much evidence against sweat-gland origin for pale epithelium and in favour of its derivation from normal mammary structures. From a practical point of view, the important issues—the formation of cysts lined by the pale cells and the relation or association of these with malignant growth in the breast—are more obvious. The cystic breast is and remains a serious clinical problem. As SHIELDS WARREN [4] points out, there are no generally accepted data which tell the surgeon what risk a patient takes if a focus of "chronic mastitis," which almost invariably shows some cyst formation, is not removed. For all cysts in the breast are not pale cysts, though these produce the typical cystic tissue, with its possibly doubtful outcome. EWING [5] held that 25% of mammary cancers were "sweat-gland carcinomas"; FOOTE and STEWART,[6] accepting a theory of apocrine metaplasia for pale epithelium, recognised an incidence of only 1%. But the coincidence of pale epithelium and malignant growth does not imply a sequence of development. There are good grounds for maintaining that pale epithelium, at any stage, indicates a degenerative change in normal cells which leads to progressively enlarging cysts, with eventual cell atrophy and permanent quiescence, though more follow-up data are needed in these cases. Such a conclusion does not, however, solve the problem of the cystic breast and its appropriate treatment. Especially in the older patient, cyst formation may screen the genesis and slow emergence of cancer in gland structures which show no pale epithelium and cystic dilatation. This is the essential problem of "chronic cystic mastitis" and its suspected "pre-cancerous" nature, a problem of clinical diagnosis and appropriate treatment which still awaits solution.

4. Warren, S. *Arch. Path.* 1940, 29, 295.

5. Ewing, J. Neoplastic Diseases. Philadelphia, 1928.
6. Foote, F. W., Stewart, F. W. *Surgery*, 1946, 19, 74.

Annotations

U.S.S.R. LEAVES THE WORLD HEALTH ORGANISATION

Russia, the Ukraine, and Byelorussia have withdrawn from W.H.O., the only specialised agency of the United Nations to which they have belonged. The Russian cable to Dr. Brock Chisholm, the director-general, said that the health ministry of the U.S.S.R. is dissatisfied with the organisation's work:

"Tasks connected with international measures for the prevention and control of diseases and with the spreading of the achievements of medical science are not being accomplished by the organisation satisfactorily. At the same time, maintenance of the organisation's swollen administrative machinery involves expenses which are too heavy for member States to bear. All this shows that the direction taken by the activities of the organisation does not correspond to those tasks which were set before it in 1946, at the inaugural conference of the organisation. In view of the above, the Union of Soviet Socialist Republics no longer considers itself a member of this organisation."

In his reply, Dr. Chisholm pointed out that the constitution of W.H.O. makes no provision for such withdrawal, and suggested that the Russian representatives should present their views to the session of the executive board, opening in Geneva last Tuesday.

"It is considered premature," he said, "to have expressed dissatisfaction with the implementation of the aims of the constitution by W.H.O. after only four months of organisation work in 1948 and a few weeks of 1949. W.H.O. is only now emerging from the organisational period. The first year programme for 1949 is now operating within the limits prescribed by the first Health Assembly. The proposed programme for 1950, to be discussed at the third session of the executive board, provides for large-scale control of epidemics by eradication and extensive strengthening of national health services which would meet your point of view. Your advice on this programme is highly desirable, your participation in the board meeting is essential, and I propose that I visit Moscow for fuller discussions immediately after the executive board in early March. I await your invitation."

The Russian decision, which will be received with deep regret, cannot be based solely on the reasons given, and must therefore be explained otherwise. The three Soviet republics signed and ratified the constitution of W.H.O. with every appearance of willingness to keep its work clear of the grosser forms of political interference and to join fully in its technical activities. But the hopes thus aroused have gradually faded. First it became clear that the Iron Curtain was not to be lifted for W.H.O.: no foreign experts were allowed into the country and no fellowships for study outside Russia were requested, though the Ukraine and Byelorussia have accepted large quantities of medical books and periodicals. Next, despite every encouragement, no Russians were nominated by their government for posts in the secretariat and none were appointed to expert committees, even when the U.S.S.R. had itself asked for Russian participation. Last November the Russian members failed to attend the second session of the executive board; communications have not been answered; and the 1949 contribution of the three Russian countries to the W.H.O. budget (£87,500 out of the total of £1,250,000) has not been paid. It looks therefore as though the Soviet Union never intended to become deeply involved and was prepared to withdraw at any convenient moment. Why then has the present time been chosen? The withdrawal—so grave in its implications—may be seen in Moscow as merely the move of a pawn in the political game. A more relevant motive, however, would be that Russia feels the need of a valid reason for opposing the fulfilment of President Truman's "fourth point" in the field of health. The Marshall plan would have been acceptable, according to the U.S.S.R., had it been implemented through the United Nations. Now, in the President's speech, the Russians may see another Marshall plan, for health, which would be carried out by a specialised agency of the United Nations and which could therefore not be logically opposed unless W.H.O. was said to be so inefficient and undesirable that the U.S.S.R. could not belong to it.

If there was one subject on which continued coöperation with the West should have been possible, it was medicine; and we do not doubt that many in Russia will be dismayed at this further retreat from realities. Time will show whether the other members of the Cominform will feel obliged to move in the same direction.

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HUMAN NUTRITION AT OXFORD

IT is perhaps curious that there has been little academic support in this country for the study of human nutrition, though a great deal of attention has been paid to the study of nutrition in animals. Distinguished work in the latter field has been done at Aberdeen by the Commonwealth Bureau of Animal Nutrition and Rowett Research Institute, at Cambridge by the Dunn Nutritional Laboratory and Animal Nutrition Institute, and in London by the division of nutrition in the Lister Institute of Preventive Medicine. Other departments have interested themselves in animal nutrition because of the light which such basic studies shed upon their particular subjects; the biochemical researches of Gowland Hopkins at Cambridge and of R. A. Peters at Oxford are notable examples. Research into human nutrition can in fact seldom succeed without complementary animal experiments. Progress in our knowledge of animal nutrition had to precede fundamental studies in man; and the comparatively small amount of research on man in this country has been done mainly in laboratories concerned with wider studies, such as those of E. P. Cathcart, C. G. Douglas, and R. A. McCance. Important contributions to animal nutrition with a direct application to man have been made by Sir Edward Mellanby, secretary of the Medical Research Council; and recently the council created a unit of human nutrition under Prof. B. S. Platt.

According to Lusk,[1] by their food policy a small group of nutritional experts in the Royal Society saved this country in 1917–18. Lusk drew attention to the inadequate support of the study of human nutrition in the United States, pointing out that the annual budget of $50,000 of the nutrition laboratory of the Carnegie Institute, Washington, was only 0·0004% of the annual American expenditure on food and one-thousandth of the cost of a battleship: "as enlightenment grows, let us hope for fewer battleships and better supported laboratories." Enlightenment grew slowly in this country, and in 1937 J. C. Spence[2] concluded that "it is a pressing need that in some of our universities there should be set up departments for the study of human nutrition."

After discussions with the Ministries of Health and Food the Oxford Nutrition Survey was started early in 1941, and it was later taken over by the university. Its functions, defined by a university decree in 1942, were: (1) to investigate economic, dietary, clinical, and biochemical methods of assessing the state of nutrition in human subjects; (2) to test, develop, and apply such methods and to give training in their use; (3) to conduct for the Ministry of Health mobile surveys relating to the nutritional state of samples of the population. It was directed by Dr. H. M. Sinclair, and managed by a committee that included Sir Wilson Jameson, Sir Jack Drummond, Sir Robert McCarrison, and the university professors of social medicine (J. A. Ryle), biochemistry (R. A. Peters) and physiology (E. G. T. Liddell). Its main sources of finance were the Rockefeller Foundation, the Ministry of Health, the Medical Research Council, the Nuffield Provincial Hospitals Trust, and the university. As Sinclair[3] has pointed out, progress was at first slow because the suggested methods of assessing nutrition were mostly so uncertain that as many as possible had to be included; to obtain quicker results a mobile team of three was formed which examined about 70 families in two months. Later, more rapid methods were evolved. For instance, the survey was invited by the Netherlands government in April, 1945, to advise upon the famine in Western Holland. Two mobile laboratories were equipped in three weeks; and with the help of Dutch scientists some 3500 subjects were examined[4] and some 20,000 biochemical estimations were made[5] in six weeks. Immediately afterwards the director was invited to take two teams to the British zone of Germany. A central laboratory was set up in Düsseldorf, and teams operated in various parts of the zone; a large body-weight survey was also organised, the results being computed at a Hollerith organisation formed in Düsseldorf. The survey was an ad-hoc war-time organisation concerned mainly with obtaining public-health data needed by the Ministries of Health and Food. During the war neither academic research nor writing-up for publication the voluminous results was justified: the accumulated findings in England, the Netherlands, and Germany will no doubt be published soon. But such applied nutrition is a function of Ministries rather than of university departments, which are concerned with fundamental research. When the Oxford Nutrition Survey ended, the university accepted from Sir Henry Wellcome's trustees a generous offer of £25,000 to house and equip a laboratory of human nutrition[6]; but later the university was unable to use the money. Last week, however, congregation unanimously approved the establishment of such a laboratory, with the aims of promoting the scientific study of human nutrition and collecting and integrating existing knowledge. Fundamental research is to be conducted into the problems of human nutrition which have their origin in physiology, biochemistry, pathology, anthropology, or clinical science, and field research may be undertaken, either here or abroad, in connexion with these problems. The laboratory is temporarily accommodated at the Churchill Hospital and directed by Dr. Sinclair.

It is fitting that such a department should be established in Oxford, where its studies may be integrated with the distinguished work of Peters upon animal nutrition and of Douglas upon metabolism, and where a wealth of material has already been collected by the Oxford Nutrition Survey.

1. Lusk, G. Elements of the Science of Nutrition. London, 1928.
2. Spence, J. C. *J. R. sanit. Inst.* 1937, **58**, 61.
3. Sinclair, H. M. *Amer. J. Publ. Hlth*, 1944, **34**, 828.
4. Sinclair, H. M. Enseignements de la guerre 1939–1945 dans le domaine de la nutrition. Liége; pp. 75–95.
5. Oxford Nutrition Survey: Preliminary Report on Nutritional Surveys in the Netherlands conducted during May and June, 1945, at the invitation of the Netherlands Military Administration. 1945.
6. See *Lancet*, 1947, ii, 116.
7. Maternity in Great Britain. London, 1948. See *Lancet*, 1948, ii, 813.

ANALGESIA IN CHILDBIRTH

ON March 4, Mr. Peter Thorneycroft, M.P., will introduce into the House of Commons a private member's Bill on analgesia in childbirth. Since 1946 the course of training for midwives has included instruction in how to use the gas-and-air method of analgesia; but there are many practising midwives who qualified before 1946 who have not yet had an opportunity to get such instruction, though all are entitled to it whenever they can be spared to take a course. Moreover the apparatus is too heavy to carry on a bicycle and many local authorities do not provide their midwives with cars. Thus though every mother has the right, in theory, to relief of pain in childbirth, her chances of getting it depend on many variables.[7]

The National Birthday Trust Fund, which has worked for 21 years for the relief of labour pain, is strongly supporting the Bill. This proposes that within three years of the Act being passed any woman who has not been instructed in giving analgesics, or who, after instruction, has not attended prescribed refresher courses, should not be allowed to practise as a midwife, and that she should be fined for contravening this law; and that every local authority should provide apparatus and sufficient drugs for the administration of analgesia, and means for the transport of such apparatus to the

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patient. In effect this would probably mean, at present, that the midwife would have a gas-and-oxygen apparatus and a car to carry it, and herself, to the case; but it is widely hoped that some less cumbersome apparatus will soon be available for the giving of analgesia.[8] Even so, every midwife needs a car to get her about. Her life is exacting enough in any case, without the strain added by cycling—sometimes long distances through country lanes—at night and in all weathers. The Bill also provides that those who control or manage hospitals or maternity homes should provide sufficient apparatus and drugs for the purpose, and shall be penalised if they fail.

TOO MUCH GASTRIC MUCOSA

SYMPTOMS ranging from severe epigastric pain to mild dyspepsia may, in the view of Cove and Curphey,[9] arise from recurrent prolapse of redundant gastric mucosa through the pylorus. They regard the condition as not very uncommon, and have diagnosed it in 22 patients with abdominal symptoms out of 650 whose upper digestive tract was examined. The evidence for the prolapse rests not on clinical findings, which are admitted to be variable and not pathognomonic, but on radiological findings and direct examination of the pylorus at operation. Cove and Curphey suspect mucosal prolapse when routine treatment for peptic ulcer has failed, or when no other lesion is found radiologically to account for severe gastro-intestinal bleeding. On physical examination, apart from mild tenderness in the pyloric region, there is only one distinctive sign, and that is not always present. A soft doughy freely mobile tumour, which disappears under pressure, may be palpable, giving a sensation like the reduction of a hernia in the groin. This sensation is due to the reduction of the mucosa through the pylorus back into the stomach. In severe cases the symptoms suggest partial pyloric obstruction, with intermittent epigastric distress and cramping pain. Milder symptoms may be a sense of fullness, heart-burn, vomiting, or nausea. There is no definite relation to food. In a few cases gastro-intestinal bleeding, evidenced by severe hæmatemesis or persistent occult blood in the stools, has been the main feature.

The average age of the 22 patients was 49 years, the youngest being 26 and the oldest 64. The diagnosis has usually rested on radiological demonstration of a filling defect near the base of the duodenal cap. This defect is central in position and most often lobulated and mushroom-shaped. The gastric rugæ may be followed into the defect, and there is no spasm or irritability of the duodenum. The defect has been more definitely seen with the patient lying down than in the vertical position.

The suggestion is that cases of gastric mucosal prolapse have been masquerading as duodenitis, duodenal ulcer, or some other established clinical entity. Cove and Curphey advise medical treatment for most cases, though they grant that there is no reason why this should effect a cure. Small feeds of a bland diet may relieve the symptoms. Sometimes rest in bed, with freedom from nervous tension, and abstention from alcohol, tobacco, and caffeine, is advised. Operation is reserved for patients with severe and intractable symptoms, vomiting bad enough to produce loss of weight, or bleeding. Palpation of the pylorus at operation is not necessarily conclusive, and the diagnosis has not always been firmly established till the antrum has been opened and the mucosa picked up in Allis forceps. The operation recommended is antrotomy, with excession of redundant mucosa, combined with some form of pyloroplasty. In 5 cases the results of this operation are said to be good.

8. *Lancet*, Feb.19, p. 312.
9. Cove, A. M., Curphey, W. C. *Surg. Gynec. Obstet.* 1949, **80**, 108.

The cause of the prolapse is not known. Cove and Curphey think that it is associated with hypermotility of the mucous membrane on the muscularis mucosæ, and that some form of hyperexcitability of the muscularis is to blame. It will be interesting to hear whether our radiologists have noted this condition, and whether our surgeons agree that it might explain some cases of persistent dyspepsia in which peptic ulcer has been suspected and not confirmed by radiography.

MORE ANTI-VITAMINS FOR LEUKÆMIA

NOT long ago preliminary results were reported with aminopterin—a folic acid antagonist—in the treatment of acute leukæmia.[1] A favourable response was noted in 10 out of 16 patients, but the longest remission had lasted only 43 days. Nothing further has been published on this treatment, but we understand that the results have not, in the long run, been encouraging. Now another anti-vitamin is being tried—desoxypyridoxine—which antagonises the action of pyridoxine, vitamin B_6. The use of this material is based on animal experiment. Cartwright, Wintrobe, and their co-workers [2] found that swine fed on a pyridoxine-deficient diet developed severe anæmia, among other things; dogs similarly treated also became anæmic.[3] Stoerk and his colleagues [4] noted that pyridoxine deficiency caused involution of lymphoid tissue in rats. All this suggested that, in these animals at any rate, pyridoxine was an essential factor for maintaining the proper function of blood-forming tissues. Stoerk [5] then showed, first, that lymphosarcoma transplants would not take in mice fed on a pyridoxine-deficient diet, and secondly, that if mice with flourishing transplants were transferred to a pyridoxine-deficient diet and given desoxypyridoxine the transplants regressed.

The next step was to try similar measures on patients with lymphosarcoma and acute leukæmia. Pyridoxine deficiency is not known to exist naturally in man, and it is not easy to produce artificially; even with American resources, the food making up the diet is described by Gellhorn and Jones [6] as of "a chalky consistency and flavour which rapidly became extremely distasteful to the patients." They at first gave desoxypyridoxine in a dose of 25 mg. per kg. of body-weight thrice daily; but there were unpleasant reactions—for instance, one patient lost consciousness, became cyanotic, and had convulsive movements of the limbs. The dose was therefore reduced to 2·5 mg. per kg. thrice daily. Six patients were treated on this régime, and a fortnight of it was as much as they could stand. The results were completely negative. There was no effect on lymphoid tissue, and the régime had no potentiating effect on nitrogen mustard treatment. Gellhorn and Jones conclude that the treatment has no practical value.

Here is yet another lesson that the mechanism of control of hæmopoiesis in man is different from that in animals like pigs, dogs, rabbits, and rats. In this particular branch of medicine, experimental results in small animals have rarely been transferable to human therapeutics. Even when the results have apparently been successful, the success has more often been due to accident than to design. Thus Whipple showed that feeding liver had a beneficial effect on the posthæmorrhagic anæmia of dogs; Minot and Murphy gave liver to their pernicious anæmia patients and the result was startling, but quite different from the effect of liver on

1. See *Lancet*, 1948, ii, 540.
2. Cartwright, G. E., Wintrobe, M. M., Buschke, W. H., Follis, H. R. jun., Suksta, A., Humphreys, S. *J. clin. Invest.* 1945, **24**, 268.
3. McKibbin, J. M., Shaefer, A. E., Frost, D. V., Elvehjem, C. A. *J. biol. Chem.* 1942, **142**, 77.
4. Stoerk, H. C., Zucker, T. F. *Proc. Soc. exp. Biol., N.Y.* 1944, **56**, 151.
5. Stoerk, H. C. *J. biol. Chem.* 1947, **171**, 437.
6. Gellhorn, A., Jones, L. O. *Blood*, 1949, **4**, 60.

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dogs. Similarly, folic acid was found to stimulate the production of granular leucocytes in rats; and Spies and his colleagues can hardly have deduced from this that folic acid would have a specific effect on human megaloblastic anæmias. These happy accidents—twenty years apart—have encouraged many more trials like the one with pyridoxine, and most of them have only demonstrated how misleading animal experiment can be in this field.

ZOSTER AND CHICKENPOX

THE relationship of varicella and herpes zoster is still not quite certain. There seems little doubt that varicella in children sometimes induces zoster in adults, and that zoster in children or adults has often caused outbreaks of varicella in children. Moreover, varicella and zoster may both be present in the same child at the same time. Zoster vesicular fluid has also been injected into children, and a disease closely resembling varicella has followed. The intranuclear inclusions and the histology of the lesions in the two diseases appear to be identical. With so much to be said for the identity of the two viruses some people may overlook the awkward differences. The age incidence, clinical picture, epidemiology, and degree of damage to the central nervous system, together with the occurrence of zoster in isolated communities where varicella has never been recognised, may all disturb the conscientious unitarian. In these circumstances the laboratory should give a clear answer; but unfortunately neither zoster virus nor varicella virus readily infects animals, nor does either grow in the developing hen's egg. Neutralisation and agglutination tests with the two viruses have not established definitely their antigenic relationship. Stokes [1] has suggested that the general population is almost universally infected at an early age with varicella virus and that resistance is permanent. Sometimes however the virus develops neurotropic properties, and it may then remain within the nerve cells of a few people in the same way as herpes simplex virus maintains a symbiotic relationship with ectodermal cells. In adult life exposure or trauma may cause localised virus activity along posterior root fibres with subsequent development of zoster lesions. This view has obvious defects and entirely lacks experimental proof, but it is a good basis for discussion.

On the morphological side Nagler and Rake [2] describe the bodies of varicella under the electron microscope as brick-shaped and in every way except size resembling the elementary bodies of the other pox viruses. The average measurements were 210 by 243 μ. Rake et al.[3] have now studied the virus particles in zoster lesions and these gave average measurements of 196 by 218 μ—that is, rather smaller than those of varicella. In general, however, the elementary bodies of the two diseases were similar both by direct vision under the electron microscope and after the use of the shadow-casting technique. In one instance fluid was examined from a patient with zoster who initiated an outbreak of varicella and the virus obtained from the zoster and from the varicella appeared identical. Of practical importance was their observation that virus particles were abundant in zoster fluid taken 12 hours after the appearance of the vesicles, whereas fluid collected 48 hours later contained very few. Farrant and O'Connor [4] in Melbourne have also been studying the viruses of zoster and varicella with the electron microscope. The profile of the varicella virus particles in their micrographs is roughly circular, but measurements showed that they were oblate and they suggest that the particles may collapse on drying at room temperature. Measurements made by the two sets of workers show differences, but size, as Farrant and O'Connor point out, largely depends on the mode of preparation of the specimen for examination. In general the electron microscope studies support the view that the viruses of varicella and zoster are the same, but those who prefer to doubt still have cause.

1. Stokes, J., in Viral and Rickettsial Infections of Man. Edited by T. M. Rivers. Philadelphia and London, 1948; p. 398.
2. Nagler, F. P. O., Rake, G. *J. Bact.* 1948, **55**, 45.
3. Rake, G., et al. *Ibid*, **56**, 293.
4. Farrant, J. L., O'Connor, J. L. *Nature, Lond.* 1949, **163**, 260.

WHAT WICKHAM DESCRIBED

THE physician must always bear in mind the diagnostic significance of physical signs; less often need he consider them from any other point of view. Yet he might more often ask who described some particular sign and when; what is the exact method of its production; and how it can be correlated with the underlying pathology. Wickham's striæ in lichen planus may be taken as an example of a well-known sign, the original description of which is rarely consulted. Louis Frederic Wickham was a Parisian dermatologist (1861–1913), and it was in 1895 that he described in detail [1] the striæ which bear his name. He made it clear that they might take many forms: "... they intersect the surface of the papule in every direction, in the form of small bands forming sometimes star-shaped figures, sometimes a main streak with lateral tributaries; sometimes there is a single stria; on some papules one sees dots either isolated at the periphery or at the centre ..." The striæ were, he said, "a sign truly pathognomonic of the disease." Wickham admitted that the striæ had previously been mentioned briefly by Ziemssen, by Hardy, and by Brocq, but none of these had emphasised their diagnostic value. Wickham made no reference to histological appearances; Darier [2] subsequently explained the striæ as due to a localised thickening of the granular layer. Darier also looked on the striæ in lesions of lichen planus on the mucous membranes as of similar origin. These views are now generally accepted; the pearly appearance of the epidermal edge in a healing granulating wound is also known to be due to the cells of the granular layer. Does this change in the granular layer or any other feature of the pathology throw light on the ætiology of lichen planus? Unfortunately it does not. The striæ have been noted in some cases of "tropical lichenoid dermatitis" [3] which occurs in about 3 out of every 2000 persons taking mepacrine. This fact must be considered an important part of the evidence identifying this condition with lichen planus, from which, indeed, it may sometimes be clinically indistinguishable. This similarity has fortified in their belief those who regard lichen planus as a toxic eruption. Some, on the other hand, believe that it is an infection. These two views are not necessarily incompatible, but it must be admitted that little more is known about ætiology and specific treatment now than when Wickham described his striæ 54 years ago.

1. Wickham, L. F. *Ann. Derm. Syph., Paris*, 1895, **6**, 517.
2. Darier, J. Précis de Dermatologie. Paris, 1909.
3. See leading article, *Lancet*, 1945, ii, 711. Bagby, J. W. *Arch. Derm. Syph., Chicago*, 1945, **52**, 1. Nisbet, T. W. *Ibid*, p. 221. Schmitt, C. L., Alpins, O., Chambers, G. *Ibid*, p. 226. Singh, I. *Brit. J. Derm.* 1948, **60**, 90.

THE SURGEON-GENERAL'S CATALOGUE

WITH the growing unwieldiness of medical literature doctors have come to lean more and more heavily on the survey of publications which the generosity of the American Congress, and the industry of the Army Medical Library at Washington, have made available through the Index Catalogue of the books, pamphlets, and journals on the library shelves. The first series of the catalogue begun to appear in 1879. The fourth, which was started in 1936, has continued despite the difficulties of the last twelve years, and is now, under the editorship of Dr. Claudius F. Mayer, half-way through the alphabet. The tenth volume, M-MEZ, has lately appeared and can be sure of its decennial welcome.

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The Act in Action

6. HEALTH CENTRES NOW?

To the general practitioner section 21 of the National Health Service Act, dealing with health centres, conveyed promise of a new and fuller form of practice in which burdens would be better adjusted. The increase of these burdens since July 5 has made such adjustment obviously necessary if the service is to run smoothly. Yet so far only one centre is being constructed. With sharpening clarity practitioners are asking whether the Ministry of Health, in its preoccupation with the hospital services, is paying enough attention to general practice, which seems likely to deteriorate unless action is taken to compensate for the new strain imposed by the Act.

A year ago the Minister of Health issued to local authorities a circular [1] which still governs policy. In this he said that though centres would be a "key feature in the general reconstruction of the country's health services," a programme for their general provision would be out of the question for some time; conversion of existing buildings was largely impracticable through lack of suitable accommodation and would in any case jeopardise the attractiveness of the conception. Where centres were urgently needed, proposals might be advanced; but the circular relieved local authorities, for an indefinite period, of their duty to submit plans.

Since then the construction of one centre—at Woodberry Down, London [2]—has been approved: it is scheduled for completion in two years. The provision of nine further centres in London—one to each of the nine divisions in the London County Council's area—has also been approved in principle. And a committee of the Central Health Services Council has been set up to advise on the whole subject.[2] So much for official action.

Meanwhile the considerable thought given to this theme has been epitomised in the report of a special committee of the British Medical Association [3]; and two series of articles have appeared in these columns [4] which indicated that no hesitation about design need delay experimental construction. (Birmingham settled on a design as early as 1943.) The main deterrents appear now to be shortage of building materials, indecision about function, and administrative difficulties.

THE PRACTITIONER'S CLAIM

Swelling surgery attendances have made practitioners, especially in industrial areas, increasingly alive to the potential blessings of the health centre [5]; and the need, in present-day circumstances, to remove the busy doctor's practice from his home has been made very clear by a peripatetic correspondent.[6] According to one estimate—not disputed by the Birmingham Executive Council—the medical work now done by the doctor in his own surgery could be done in a health centre in three-quarters of the time. Such a gain, together with the resources of the centre, would enable the practitioner himself to treat patients—such as those with cut scalps or discharging ears, or in need of dressings or injections of penicillin—who now commonly go to hospital. Reference to hospital without intrinsic need has been deprecated by the Minister [7]; but he has given no undertaking to provide, in centres, the means to end it. To the already hard-pressed practitioner a severe epidemic would have been almost welcome this winter as a stimulus to Government concern for his work.

Improved medical attention would not be the only advantage of the centre. Waiting-rooms, often on the small side even before last July, now commonly spill their human contents on to the pavement. Why, it is asked, does a Ministry which shows acute interest in the comfort of hospital outpatients,[7] view with seeming nonchalance this deplorable state in a different branch of the same service? As a general practitioner and chairman of a hospital management committee, Dr. Louis Comyns, M.P., said [8]:

> "Before the start of the service doctors' waiting-rooms were reasonably adequate; but during the past six weeks patients have not infreqnently been seen to be waiting about on the pavement. The deficiencies of the hospital service are being publicised and an attempt made at their rectification, but nothing is being said or done for the early improvement of conditions in general practice. In my experience the feeling among practitioners is one of great and growing frustration."

PUBLIC-HEALTH SERVICES

In centres the quality of practice would immediately gain by the opportunities for close association of the practitioner with health visitors, home nurses, and others working for the local health authority. To medicine as a whole the ultimate gain may be still more important if through centres the maternity and child-welfare and school-health services can be interwoven into general practice. These services, with prevention as their aim, have grown up through the endeavour of public-health officers, who have done their work well. The services were, however, brought into being as a stop-gap, to safeguard the health of important sections of the population which were then unable by right to seek the advice of a general practitioner. Nowadays it is axiomatic that preventive medicine is not one separate field and curative medicine another; both should come within the purview of the family doctor. The National Health Service Act makes possible the achievement of this important objective; but it is hard to see how it can be achieved except through health centres, and each year that passes without centres defers its attainment by so long. Certainly there are difficulties. Medical officers of health, the scope of whose work has already been greatly reduced, naturally cling to what they still have; and they will cling to nothing more fiercely than their clinical services, of which they are proud. They and their assistants have long experience and expert knowledge in this field; moreover they have the "preventive" outlook, and they are adept in health education which is an important part of prevention. But in the long run the care of the child ought to be undertaken by practising family doctors, and the proper course is to encourage suitable practitioners at health centres to undertake part-time work at the associated clinics. The work of the clinic doctors would gain if they, for their part, took a share in group practice.

A possible peril to progress along these lines is that centres may be started by medical groups in existing buildings which have space for nothing more than the communal surgery. Proposals to make a beginning in this way are tempting; and perhaps they should sometimes be accepted as an expedient to relieve the practitioner. But they do not satisfy the concept of a true health centre; and temporary administrative measures, like temporary buildings, often prove perniciously permanent. The same risk is inherent in new provision for local-authority services without inclusion of general practitioners.

SOME OBSTACLES

How will patient and doctor view centres? It has been represented: (1) that some patients, accustomed to

1. Circular 3/48. See *Lancet*, 1948, i, 161.
2. *Lancet*, Jan. 29, p. 196.
3. *Brit. med. J.* 1948, ii, suppl. 107. See *Lancet*, 1948, ii, 464.
4. *Lancet*, 1946, i, 392, 393, 471, 515, 550, 586, 665; *Ibid*, 1947, i, 32, 78, 114, 154, 189, 228.
5. *Ibid*, 1948, ii, 823.
6. *Ibid*, Feb. 12, p. 281.
7. *Ibid*, p. 289.
8. Personal Communication.

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keeping their visit to the doctor a private affair, will dislike the slightly enhanced publicity; and (2) that the general practitioner, as an individualist, will not take easily to group practice. The weight of these objections can be tested only by experience.

Other questions, however, will have to be answered before the centre is opened. One—small but important—is how much rent should be charged to the doctor. A second—and harder—is whether the practitioner should be allowed to conduct private practice from the centre. The Minister's answer is thought to be No. He is believed to interpret the Act as not permitting him to sanction such practice, though the Act does not seem to prohibit it. Many who have the future of the service at heart hope that he will reverse this decision. Private practice—if only in the form of life-assurance examinations and so on—is likely to survive for some years at least; and nothing will do more to deter a doctor from entering the centre than the knowledge that he will still have to maintain a private consulting-room. Moreover, in visiting centres private patients should see a favourable aspect of the service which might make them more willing to join it.

If these points are in doubt, two things at least are certain: (1) that the practitioner must be a willing participant; and (2) that he must work in true partnership with his colleagues in the building. Those who recognise that open competition for patients would kill the scheme may be led to suggest that the only solution is for doctors in centres to be paid by salary. But here and there groups are giving thought to establishing themselves in voluntary partnership in centres; and a happy outcome of their experiment might change the outlook of others. Nevertheless, it would be foolish to deny that this is probably the most formidable stumbling-block of all.

TOO MANY COOKS?

Before construction starts, the wishes of many other parties have to be consulted and met. About the patients' attitude there is little doubt: for the most part they favour the idea. Most local authorities—which have to foot much of the bill—are also interested, as a matter of civic pride, in setting up centres. Executive councils are unlikely to resist such a movement; but local medical committees, mindful of responsibility to every doctor in the locality, have to make sure that those who are to work within the centre will not gain undue financial advantage over their colleagues who remain without.

THE FABRIC

Perhaps unfortunately for the present purpose, the Minister of Health is also the Minister for housing. Building materials, especially steel, are scarce; and clearly the amount allotted to health centres will depend on the priority accorded them, compared with hospitals and schools, flats and factories. Supplies are improving somewhat, and immediate experiment with centres along the lines suggested by the B.M.A. committee is being urged with increasing vigour; large-scale construction might start 2–3 years after completion of the pilot centres. Other critics of the present policy would go further and proceed with immediate building wherever the need is urgent; and of those who hold this view some are willing to accept prefabricated construction rather than none at all.

In this country few voices speak in defence of temporary prefabricated structures—and hardly any among local-authority officials. It is contended that the internal walls of a prefabricated building, which provide the equivalent of only $4^1/_2$ in. brick (compared with 9 in. in ordinary houses and 14–18 in. in hospitals), would allow sound to travel almost unmolested from one consulting-room to the next. Furthermore, prefabricated structures, being of only one story, demand ground-space; and ground-space is seldom easily found in the districts most in need of centres. Finally, what of the dignity of the health-centre idea? Would not the ungainly "prefab" make people think that health centres are designed to provide second-rate "utility" medicine?

So the argument goes. It can be retorted that prefabrication, with its opportunities for altering internal walls, is the method of choice in the experimental period. And which would be better—to have one permanent centre two years from now, a further nine in London in perhaps five years, and more in the unnamed future, according to the present programme, or to have two or three score prefabricated structures up and in operation within, say, two years? As to appearances, Birmingham, well known for its civic pride, has proposed a plan for just such a building. Can we not drag ourselves out of the slough of planning on to the firm ground of action?

WHAT SHOULD THE CENTRE CONTAIN?

Of the further elements which may be causing hesitation, one is doubt about the units that should be incorporated. Official opinion is thought to favour at least a trial of full dispensary services in one or more centres, though at Woodberry Down the smallness of the space allotted to a "drug store" plainly precludes such a test. There are questions, too, of the desirability of including a physiotherapy department, X-ray apparatus, and a clinical side-room. There is uncertainty about which, if any, specialist services should be included; and there is the borderline case of the foot clinic, for which space has been provisionally allotted at Woodberry Down. Here again the right answers—which will vary with the area—can probably be found only by trial.

FURTHER RESEARCH

The views of most general practitioners are perhaps best summed up in John Hunter's impatient remark to Jenner: "Why think? Why not try the experiment?" If there is to be further research, it might follow three lines:

1. *An investigation of the under-doctored areas.*—The two main deterrents to doctors starting practice on their own are (*a*) the difficulty of finding houses suitable for the conduct of practice; and (*b*) their high cost. Nowadays, when doctors die or retire their houses seldom come on the market; and in some districts suitable houses are simply not to be found. When they are found, they are necessarily large and in prominent positions, and may cost upwards of £6000. The immediate provision of health centres in under-doctored areas (which also, generally speaking, have the greatest genuine need of centres) would attract practitioners by enabling them to live in a more modest home, which might also be more easily obtained, and to escape the severe initial cost of a house from which to practise. Analysis of the experience of the many practitioners now at a loose end would confirm or refute this argument.

2. *A general-practitioner "job-analysis."*—If, as Birmingham believe, 25% of the time now spent by the practitioner on medical duties can be saved in health centres, this is a serious consideration which may well affect the priority accorded to their construction.

3. *A survey of "user-reaction."*—It seems curious that the only centre yet firmly promised is to be set up in a district with a fluid and growing population. The establishment of a centre in a district with long-established practitioners serving a stable population would enable patients to compare the two techniques; it would also enable medical officers of health and practitioners, together for the first time, to relate their new and nearer gaze to their former detachment.

So far as general practice is concerned, inaction is daunting those who have constantly supported the Act, while those who have opposed it are finding their worst hopes fulfilled.

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Special Articles

FELLOWSHIP FOR FREEDOM IN MEDICINE

AT a meeting in London last Saturday the fellowship discussed its articles of association and its future policy.

Lord HORDER, the chairman, said that the number of members was already 2200, though the fellowship had only been in existence three months and had made no general appeal to the profession to join. Donations had been received from members but money offered by members of the public had not been accepted.

The general situation in regard to medicine had deteriorated considerably. In face of this situation it was clear that the fellowship had a good moral effect on the profession, on the public—and on the B.M.A. "We are not in opposition to any body," continued Lord Horder. "We have a particular job to do, and we will get on with that job. If the B.M.A.—which is the big body through which doctors have voiced their opinions in this country—fails to voice those views, or voices no views at all, the fellowship will do something about it." The activities of the fellowship were being watched with interest outside Britain, especially in America.

Dr. J. A. MOYSE declared that Parliament was not all-powerful; it was the electorate which was all-powerful. The fellowship should consider its political organisation. "We are not going to hide behind the skirts of our profession. We must get into politics."

Dr. MARGARET LOWENFELD urged that the fellowship should aim at a positive re-creation of medicine. The profession failed last year because it did not put forward proposals more constructive than the Minister's. She moved that the objects of the fellowship should include the making of "constructive proposals for the better organisation of the medical services of the country, in accordance with the progress of the medical profession." Lord HORDER did not favour this suggestion. "We, as standing for medicine," he said, "are available for any Government which likes to ask our advice." But the initiative should come from the Government as the administrators.—Dr. Lowenfeld's motion was negatived.

A clause which stated that an object of the fellowship was to "maintain the status of the general practitioner including his financial security" was amended by substituting "medical" for "general."

Turning to future policy, Lord HORDER said that the executive committee agreed that the National Health Service Act was a very bad Act; "but if we made repeal our main object, we should have to concentrate on that—and with what sort of hope of success?" He felt it was better to aim at drastic amendment.

Dr. C. E. TAYLOR asked whether they accepted "the nationalisation of the general practitioner." Or were they to say they accepted it, but only under compulsion? Lord HORDER commented that it would be claimed there was no nationalisation, but the Act enabled the Minister to nationalise the profession by regulation. Dr. MURDO MACKENZIE expressed detestation of the notion of the primacy of the Minister in medicine.

Dr. E. B. BROSTER queried whether the nation could afford the service, either financially or morally. Financially, initiative was being crushed by heavy taxation. "Morally, by this Act we are being turned into a 'sickness-minded population.'" The doctor had become a mixture of a "nursemaid and confidence trickster."

The meeting generally agreed to press for amendment rather than repeal.

THE MINISTER'S POWERS

Mr. NORMAN LAKE said it was disgraceful that a member of an ancient and still honoured profession should find himself forced to fight to preserve his liberty. The Minister had exceedingly great powers through rules and regulations: clause 66 showed how wide were these powers in respect of individuals. He said that, as the Minister was responsible to Parliament for the service, he must have sufficient personal power to see that it was properly carried out. Superficially that was a specious argument. But the real answer was elsewhere. It was to be found in an article by the present Chancellor of the Exchequer, which said that for Socialism to come "constitutionally" Parliament should pass general Acts and not discuss details. Because the courts sided with the people where a Minister exceeded his powers, the right of appeal to the courts against Ministerial orders should (said Sir Stafford Cripps) be abolished. The power of local authorities should be curbed by putting them under regional bodies filled with "staunch party members who will see that Ministerial orders are carried out promptly and efficiently." Civil servants should be replaced by ones of known Socialist sympathies, and the Socialist Government should decide whether to have an election or not. The connexion between Sir Stafford's article and what was happening in the health service was too great to be a coincidence. Unless the Minister's powers of appointment and control were curtailed, the profession would become subservient to political views of one sort or another.

Calling for the exemption of teaching institutions from the control of the Minister, Mr. REGINALD PAYNE said all medical teaching was now being carried out in State institutions by State servants. That had happened in Germany. So far it had not happened here in any other faculty. On the Central Health Services Council were the presidents of the Royal Colleges—and 35 Government nominees. The professional leaders had allowed themselves to become a minority in a body whose report the Minister could suppress and whose chairman was a Labour M.P. who recently declared that "for too long the needs of the people have been subservient to the needs and training of the doctor." The colleges were now controlled by politicians. The Royal Colleges should represent the highest educational, ethical, and professional principles. "In connexion with my own college," declared Mr. Payne, "the opinions of the fellows have been deliberately suppressed in relation to this Act." If something was not done, "we shall have to think of independent colleges."

OTHER PROBLEMS

Dr. A. C. E. BREACH spoke of the aim to secure a restoration of the right of ownership of goodwill in practice. "It is often said we are the spearhead in the fight for survival of the middle classes," he said. "If we are that spearhead, then this is the point of the spear." The right to ownership of goodwill affected a wide range of people, from lawyers to small shopkeepers. "If we go into this fight," continued Dr. Breach, "it will be a strenuous one, and we shall not have any political support. So what? We are not children who need political nursemaids. This is our fight. But behind us are ranked the whole middle and professional classes of the world."

A dissenting view about the buying and selling of practices came from a member speaking from the floor of the meeting. Since the doctor had received fees, what right had the doctor to take a capital sum for services which he had rendered? If consultants did not sell their goodwill, it required special justification for the general practitioner to sell his practice.

The meeting agreed by a large majority to press for restoration of the ownership of goodwill in practice, a decision which was warmly applauded.

Dr. G. M. GOODWILLE advocated grants in aid ("contracting out") towards the cost of medical services in private wards of hospitals or by private doctors. At the suggestion of Dr. A. G. HERON, the words "or in nursing-homes" were added.

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A member was loudly cheered when he said he hoped it meant that the fellowship would fight for the right of free medicines for private patients. Lord HORDER said that a test case on this aspect would come before a county court shortly, where a chemist had charged for dispensing a private doctor's prescription and the patient was suing the Minister for the money.

Dr. R. HALE-WHITE said it was generally agreed that the per-capita figure for the first 1000 patients should be considerably increased, and thereafter there be a sliding scale. The betterment figure of 20% was much too low; it should be 85%. He hoped that when the profession had decided what was a fair figure for remuneration it would not negotiate, which was only a form of bargaining, but would state the figure and brook no other.

The Wider World

NUTRITION AND HEALTH OF CHILDREN IN FIVE COUNTRIES OF SOUTH AMERICA

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3. Bolivia

Bolivia is a country of many contradictions. There are vast areas of fertile lands, which are practically uninhabited and untilled; yet large numbers of the population live only just above starvation level. Much of the food is imported, and to obtain money for this purpose Bolivia is utterly dependent on the price of tin.

Geographically three distinct regions can be recognised:

The *Altiplano* is a vast level tableland in the Andes, mostly about 13,000 feet above sea-level. Here no trees grow, but a thin scrub can nourish herds of goats, sheep, and llama; a peasant population can support a hardy existence growing cereals and roots, often by shifting cultivation on a stony soil. Around this plateau are the mountains, from which almost every metal useful to man can be extracted. Silver was the first lure, which attracted the Spaniards; but in our age tin has proved the most valuable product. The tableland cannot produce enough food for the mining and urban populations. Three separate railways run through passes down to the Pacific Ocean: they carry away the metals and bring back food.

To the east of the Altiplano there are huge *tropical plains* through which the waters drain into the Amazon and La Plata river systems. These plains are for the most part uncultivated and very sparsely inhabited. They have enormous agricultural potentials.

Separating the Altiplano from the tropical region are a number of fertile valleys, which have a *temperate* climate. They are rich agricultural lands.

Immense natural obstacles confront road-makers seeking to link the temperate zone with the tropical districts and the Altiplano. From the air I was reminded of the huge mountain barriers that have so effectively separated India from Burma. Hitherto the people of the Altiplano have looked westward and to foreign trade for many essentials. If and when roads and railways can be built linking them with the great potential agricultural wealth in the east, a new era of prosperity will begin. The first and fundamental public-health problem is transportation.

Many of Bolivia's present difficulties have roots deep in history. The conquistadores came to the country in search of precious metal. This they found. Five hundred million silver dollars are reputed to have been taken from one hillside alone near Potosi. The original culture and elaborate social organisation of the Incas was shattered. A vast agricultural community was broken up. To the native Indians, the stern evangelists offered nothing but a bare subsistence in this world and the hope of salvation in the next. In 1825 Simon Bolivar, a liberal idealist nourished by the ideas prevalent in 18th-century France, was able to sever all connexions with the effete and greedy government in Madrid; but he was unable to replace the colonial despotism by any stable system of government. Bolivia remained, and essentially still remains, a place where one comes to get rich, not to help build a healthy balanced human society.

In her many wars with her neighbours Bolivia has been invariably unsuccessful. In the last futile war with Paraguay nothing was achieved, but 60,000 men are said to have been killed or died of disease. Great quantities of treasure were expended, and only the foreign armament firms grew rich. The effects of this war on child health and welfare are manifest today: Bolivia, a rich country, is inhabited by poor people. A leading pædiatrician told me that the three basic requirements for child health in his country were "more roads, more capital, and more immigrants." Without these it must remain poor. Nevertheless I was frequently surprised to find how much individuals and small groups of people with fine ideals have been able to accomplish.

THE PEOPLE

Such statistical information as is available has been summarised in *Epidemiologia Boliviana* by Dr. Juan Balcazar, formerly professor of hygiene and now minister of health.

There has been no census since 1900, when the population was 1·77 million. The probable figure for 1948 is a little over double this, 3·59 million. Some 70% are indigenous Indians, mostly simple agriculturists and miners; 25% are mestizos, mostly artisans, clerks, and town-dwellers; and 5% are whites, mostly professional classes. Though there are only 60,000 permanent miners, many agriculturists (probably 80,000–90,000) work in the mines for four to six months of the year.

Approximately 1·7 million persons live on the Altiplano, 1·3 million in the temperate valleys, and half a million in the low-lying tropical zones. The population density for the whole country is only 3·3 persons per sq. km. La Paz, the biggest town, has about 300,000 inhabitants.

FOOD-SUPPLY

Large amounts of wheat, sugar, rice, animal fats, and vegetable oils are imported, and in addition meat on hoof comes from Argentina and Peru. In 1945 food products represented 36% of all imports—a fantastic figure for a country with rich agricultural resources undeveloped. The problem, Dr. Balcazar says, is fundamentally one of distribution not of production:

"There is abundant cattle in the Beni and it is in the Beni where the least meat is consumed. Enormous plantations of sugar-cane exist in Santa Cruz and it is in Santa Cruz where there is a great scarcity of sugar, because the major part is converted into alcohol. We have overproduction of many articles in certain zones—maize in the provinces of Chuquisaquena and Cochabamba—and the excess is used as cattle food and as fuel."

Agricultural production is determined by tradition and local custom rather than by nutritional needs.

The indigenous people of the tropical regions and the temperate valleys live on maize, potatoes, mandioca, plantains, and a variety of fruits and vegetables. In Santa Cruz I saw a tremendous variety of tropical fruits, and many other districts are equally rich. In the Altiplano the principal articles of diet are quinua, potatoes, a little wheat, and barley, and even the poorest have some access to meat, either mutton, pork, or beef.

Mention may be made of quinua, a cereal indigenous to the Altiplano and probably unknown to most nutritionists. It is a hardy crop, flourishing in poor soil. The grain is very small and resembles the small millet ragi, widely grown in South India.

HEALTH AND DISEASE

Balcazar, reviewing the meagre figures available, gives the following indices for 1944.

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Birth-rate	33·9
Death-rate (average of the eight largest towns)	28·5
Infant mortality	289·4

There can be little doubt that not more than half the children survive to reach their fifth birthday.

Nutrition.—By modern American standards the nutrition of the people is bad; but, in comparison with vast numbers of the inhabitants of Asia, most Bolivians might be much worse off. The principal defect in their diet is the very low intake of milk by all classes and in all districts. This must be largely responsible for the retarded development and small stature of almost all the children, and must also contribute to the low resistance to infectious diseases and the high death-rate of the young. The people I saw in the Cochabamba district and on the Altiplano looked sturdy and vigorous, and I doubt whether those in the countryside suffer from hunger or undernutrition, except in extraordinary circumstances; but in the big towns, largely dependent on imported foods, primary poverty undoubtedly leads to partial starvation. I saw many cases of this, though the proportion is probably not high.

Deficiency diseases are uncommon, and in none of the many hundreds of children I examined was vitamin deficiency clinically demonstrable. Pædiatricians diagnosed rickets freely in the children aged about one year on the basis of delayed dentition and late closure of the anterior fontanelle, but rachitic deformities in older children are certainly rare.

The dental condition of the children is interesting. In Santa Cruz every child examined had several grossly carious teeth, and almost all the adults have mouths disfigured either by ugly gaps or large masses of gold, according to social class. By contrast, in the Cochabamba district I saw several children with perfect sets of teeth and it was rare to find more than one or two decayed. In La Paz the position was intermediate: dental caries was widespread but seldom severe. These are only casual observations, but those interested in the ætiology and epidemiology of dental caries might find Bolivia a profitable country to study.

Infectious Diseases.—The great insect-borne diseases—typhus, plague, yellow fever, malaria, and leishmaniasis—all flourish in Bolivia. Thanks largely to the efforts of the Rockefeller Foundation, they are at the moment well controlled and probably are not responsible for more than a small proportion of the total mortality. Their existence, however, is a potential threat to health. Smallpox is kept within bounds by an energetic vaccination campaign. Tuberculosis and syphilis are widespread in the towns, and reflect the poor housing conditions and low moral standards of many of the people. Pneumonia is common, and with whooping-cough must be responsible for a large proportion of infant deaths. An intensive immunisation campaign against whooping-cough is being carried out. Gastro-enteritis is widely prevalent among infants and young children. Typhoid and bacillary dysentery are common, but several physicians told me that amœbiasis was rare. In the tropical districts intestinal infestations are widespread and perhaps present the most urgent public-health problems. A recent survey in the Santa Cruz schools showed heavy infestation with both hookworms and roundworms.

Altitude.—Bolivia shares with Tibet the distinction that a large proportion of the inhabitants live and work at altitudes above 13,000 feet. There have, of course, been many physiological studies of the acute process of acclimatisation to low oxygen pressure, but the effects of low oxygen pressure spread over many generations have probably not had sufficient attention. The possible effects on the psychology and working efficiency of mining communities might merit investigation.

Coca.—Many Bolivians, especially in the Altiplano, chew coca leaves throughout the day and can accurately be designated cocaine addicts. It is widely supposed that coca enables a man to carry out hard work at high altitudes with greater efficiency, and makes him insensitive to hunger, but that in the long run it leads to serious breakdown in both mental and physical health. Yet many experienced observers, both lay and medical, doubt the accuracy of these views. I heard the opinion that coca-chewing was, like tobacco-smoking, a dirty habit, but had no serious effects on either health or working efficiency. The extent of the habit can be judged from the fact that Bolivia is said to produce 3 million kg. of coca leaves a year, of which 85% is for home consumption. Statements both by individual observers and authoritative international conferences have mostly been adverse to coca; but no steps have been taken to attempt to control its use. A fresh assessment of the problem might be timely.

CHILDREN'S HEALTH SERVICES

The Servicio Co-operativo Inter-Americano de Salud Publica (SCISP) provides a wide variety of services. I was able to see the work of the children's clinics in four cities.

The primary work of these clinics is health education. Here is an enormous opportunity, and the doctors and nurses are tackling it with energy. The value of this work is immense. The only criticism I would make is that, on occasions, I heard advice straight from "Harvard" being given out undigested. Unfortunately what is sound common sense in "Boston" may be quite unpractical in La Paz.

The clinics are able to provide simple remedies and can undertake worming and the treatment of congenital syphilis. Small quantities of fish-liver oils and vitamin concentrates are available. SCISP has a little dried and tinned milk for distribution, but nothing like enough: it is reserved for those almost completely destitute.

A government school breakfast scheme has been initiated; but so far only 17,490 out of 187,266 school-children receive the meal. (The number of children who attend government schools is estimated at less than a third of the total number of children of school age, of whom the majority receive no formal education.) The breakfasts I saw consisted of a small bun and a mug of very thin porridge. Clearly at the moment they amount to very little: however, they are a beginning. There is no provision for extra milk, food, or vitamin supplements for pregnant women, infants, or preschool children.

Bolivia possesses a few institutions and services for children that are excellent. They can in no way cover the needs of the numerous children who require institutional or other care, but they will be invaluable as examples.

The Mining Communities.—Any mines employing 250 workers have to maintain a doctor, who, besides looking after the miners, provides medical care for their families. All big mines have a hospital attached. Thus children in the isolated mining communities receive some medical care. The food sold at the mines' stores is heavily subsidised by the mining companies. In the mine I visited, the cost of the food subsidy per shift was 80% of the average wage per shift.

CONCLUSION

The great majority of the people of Bolivia are simple agriculturists, who live in primitive conditions and have been spared the advantages of the Industrial Revolution. Unlike similar peoples in so many other countries, they do not suffer from a severe shortage of land. Thus, for the most part, they can grow a sufficiency of food for the needs of their families. Their health problems are those of a people utterly ignorant of hygiene. Their mortality-rates are high, but those who survive are sturdy peasants, apparently cheerful and happy, and not unversed in primitive arts. They rear their animals mainly for meat and wool, and obtain very little milk. An increase in the milk-supply is clearly possible and would undoubtedly improve the general health of the children.

In La Paz (and no doubt in other Bolivian towns) there is primary poverty, and a proportion of the children are severely undernourished.

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Disabilities

24. PARKINSONISM

A DISEASE from which one suffers oneself has a peculiar reality, and it enables one to learn the real action of the drugs recommended for its treatment, as distinct from the actions which are desired, expected, or imagined, or are memorised by examination candidates.

About 20 years ago the writer began to notice in himself various symptoms of parkinsonism, which were at first attributed to suggestion, as he had by chance seen a good deal of two well-marked cases of this condition. For some time he took no diagnostic steps; a tendency to fall forward in walking need not affect one's capacity to earn a living, and even a considerable amount of tremor, when a steady hand is not required, may be more annoying to other people, especially when communicated to furniture, than to the patient (incidentally, a hairdresser, and a cat wishing to sleep on one's lap, may show resentment). But extreme slowness in handwriting, due to stiffness of the thenar muscles, is not only inconvenient and time-wasting, but, when another person is waiting for what one writes, very embarrassing. Increasing inability to write at last caused the writer to consult the late Dr. Kinnier Wilson, who was then a leading authority on such conditions. His diagnosis, made, as he said, as I entered the room, was immediate and precise, and was accompanied by the rather cheerless comment "Your face isn't glazed *yet*." Possibly the condition arose during the influenza epidemic of 1918, of which the writer remembers only a period of intense sleepiness.

The treatment adopted was to take seven granules, each containing 0·5 mg. of 'Genoscopolamine' (described as N-oxy-hyoscine hydrobromide*) before breakfast. This immediately relieved the tremor and made writing possible though not easy. The good effect wears off in the latter part of the day, and for some reason a second dose is not very effectual. A trial was made of stramonium alone, but an adequate dose produces an unpleasant feeling of sleepiness and torpor and the drug was abandoned.

Some non-medicinal treatment was tried also. Exercises of the "physical jerks" type lessen muscular stiffness and produce a feeling of fitness, as they do in a normal person, but they do not really make much difference. Swimming, preferably on the back, is, to those accustomed to swim in pre-parkinsonism days, much easier than walking, and eliminates the wearisome tendency to fall forward. In deep water, one must not go on swimming until one is tired, for muscular action is then apt to stop. Curiously enough, the chief difficulty arises in shallow water, in resuming the standing position.

During the past year, after about 15 years of the medicinal treatment described above, various combinations of drugs (tinctures of stramonium and belladonna, pilocarpine, hyoscine) have been tried. Belladonna has not been used in large quantities as my physician tells me that a dose sufficient to relieve the symptoms of parkinsonism would produce unpleasant eye manifestations and excessive dryness of the mouth; but mixtures containing stramonium, hyoscine, belladonna, and a small corrective dose of pilocarpine make it possible to enhance the desired action of each drug before producing too great an undesirable effect. Moreover, tolerance to some of the side-effects will be acquired if medication is continued. The following mixture is now used, which was arrived at by trial and error (without the knowledge of the patient, to eliminate the effects of suggestion).

Tincture of stramonium	8 ml. (2 fl. dr.)
Tincture of belladonna	0·5 ml. (min. 8)
Pilocarpine nitrate..	1 mg. (gr. $^1/_{64}$)
Hyoscine hydrobromide	0·8 mg. (gr. $^1/_{80}$)
Water to 15 ml. ($^1/_2$ fl. oz.)	

The parkinsonian has difficulty in starting to walk, and in stopping when once started; these disabilities are never more insistent than in a picture-gallery, where the visitor's actions must consist of a series of starts and stops. In this matter the result of the new treatment, which one may call the "picture-gallery effect," is most remarkable; the writer was able to pay many visits to the exhibition of Indian Art at Burlington House with a degree of comfort which he had not known on such occasions for many years.

An appropriate dose removes the tremor completely; indeed, the ease with which tremor can be turned on and off suggests an excellent opportunity to investigate the metabolism of tremor. Writing becomes immensely easier, though one may never be able to write at "scribbling" speed. Another rather annoying symptom to which this treatment brings relief is that one is apt to get "stuck" and unable to move in any unusual position of strain—e.g., when picking something up from the floor. The apparently simple movement of drying one's hands on a towel, which to the patient is peculiarly difficult, becomes easy. When one is at the optimum stage of absorption of an optimum dose of the preparation in its best chemical state (the mixture is rather unstable) one may feel for a time just like an ordinary person—this is a very great success, and a very great blessing.

* * *

The treatment has certain disadvantages:

(1) An adequate dose produces considerable dryness of the mouth, and if a somewhat larger dose is taken swallowing may be impossible. This effect would provide an admirable exercise in practical physiology for students, to demonstrate the lubricating action of saliva. One must learn to take the medicine at such times that the dryness causes the minimum of trouble. Thus, if the first dose is taken after breakfast the maximum of dryness may be over before lunch.

(2) The medicine may cause a certain amount of gastric discomfort if taken without food. The relation of doses to meals must be regulated by trial. The writer takes the first dose (10 ml.) just after breakfast, at which meal strong coffee is avoided as the two together are apt to cause indigestion; the maximum dryness of the mouth is then over before midday. A second dose (5 ml.) is taken in the early afternoon, and a third (also of 5 ml.) in the evening only if it is especially desirable at that time to avoid tremor, which otherwise may reappear about 8 or 9 P.M.

(3) One cannot expect to have at the same time muscular relaxation and a sense of muscular fitness; hence the medicine produces at first a considerable lassitude. At the same time there may be an increased tendency to fall forward (actually one never does fall, however imminent such a catastrophe may seem to an onlooker), which may be a result of the relaxation. This feeling of limpness and lassitude becomes much less in a few days.

(4) The effect on accommodation is not usually noticeable if one does not think about it. If it is perceptible when accurate vision is required, as in reading any graduated apparatus, one must use a lens or additional spectacles.

* During the war this drug was very difficult to obtain, and friends in the United States gave invaluable help in maintaining a supply.

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(5) When one has become fully accustomed to the medicine, neglect to take the usual dose at breakfast-time is followed by a surprising degree of nausea and sweating. Hence it is very important to keep an adequate supply at hand.

One would advise anyone commencing the treatment to ascertain by trial the optimum dose and number of doses and their relation to meals, and on no account to be discouraged by the feelings of malaise, lassitude, and muscular limpness, which soon diminish, the first two rapidly and the third more slowly. The ultimate effect is to make walking very much easier, and enjoyable.

The writer feels deeply grateful to his physician, who has given him an altogether different life. And he would thank also those enigmatic plants of the Solanaceæ which accomplish, within the microscopic compass of their cells, organic syntheses, doubtless of value to themselves, which elsewhere would require the resources of a research institute.

Medicine and the Law

More War Pension Cases

DECISIONS on war pensions continue to accumulate. Here are three from the Scottish courts, promulgated at the end of last year. In Watson *v.* Minister of Pensions a soldier had died from myeloid leukæmia. In an earlier case (Thomson *v.* Ministry of Pensions) the court held that the tribunal was not justified in refusing a pension. The tribunal had no definite information of the ætiology of the disease and the Minister had been unable to produce evidence to negative the possible effect of Service conditions. Later it was possible to establish by medical evidence that death from myeloid leukæmia was attributable solely to natural causes, and therefore in subsequent cases the pension was refused. The widow's appeal in Watson's case had been held up in view of the Thomson case. The court sent it back to the tribunal—a step which gives her the chance of any benefit to be derived from the decision in the Thomson case but which will allow the tribunal to hear the fresh evidence now available on the attributability of the disease.

Two other cases went against the Minister. In Henderson *v.* Ministry of Pensions a soldier had suffered in childhood from otitis media. Thirteen years later it recurred in 1943. The tribunal found that the disease was not attributable to, but had been aggravated by, war service. The court awarded a pension on the ground of attributability. There had been no evidence before the tribunal that otitis media was "a continuing, latent or recurring disease," or that an attack in childhood made the patient more susceptible in later years, or that there was any connexion between the two attacks. The Minister had the onus of establishing that the 1943 attack was not attributable to war service. He had failed to do so.

Finally Duff *v.* Minister of Pensions was the case of a soldier who suffered from nervous depression. His call-up was postponed on this account; within 14 days of his joining his unit he committed suicide. The tribunal took the view that the neurotic condition was a result of the previous illness and that the fortnight of Army life had done nothing to aggravate it. It therefore refused the widow's claim to a pension. The court once more reversed the tribunal's decision. There was no evidence that Duff's Army service did not play a part in aggravating his neurotic state. The tribunal had found that his Army life was happy enough; this seemed to mean that the life would not have upset a normal man. That was not the test. The criterion was individual in its application—did Army service affect this particular man?

In England Now

A Running Commentary by Peripatetic Correspondents

THE BED BARGAIN

My partner has my list and I have his,
By some mistake each has the other's gotten.
His is a lengthy one, by gum, it is:
His patients, bellyachers feeling rotten.
My partner has my list and I have his.

His list comprises all the orotund,
The hypochondriacs, the masochists,
The psychoneurotes, and the moribund:
Of cheerful convalescents *mine* consists.
I wish I had *my* list and he had his.

* * *

Being a house-surgeon in a children's hospital had made me discount at least half of the mothers' statements about their children; even more did this apply with our son, for his mother is a nurse and consequently almost as good as a doctor at fixing imaginary ills on her own offspring. So when she rang up at lunch-time to say that young James—three weeks old, healthy, and the child of reasonably normal parents—had brought up "everything" since 6 A.M. and that she thought he had pyloric stenosis, I was suitably sceptical and patronisingly reassuring. I did, however, agree to slip home (receiving-day notwithstanding), thinking that a few sage words on the management of gastric flatulence would suffice. I was chagrined to find slight visible peristalsis, an indefinite tumour, and a very definite vomit. My reaction was "this can't happen to us"; but my chief confirmed the diagnosis, James doing his best to help by being so violently sick that he saturated the august personage with a mixture of stale milk and glucose water.

The Rammstedt's operation, done next day, went beautifully but was followed, as might be expected in a doctor's and nurse's child, by a wound infection and its corollary in babies, a refusal to feed. The infection was the result of parental laissez faire with a moist umbilicus, a policy that had not allowed for an upper abdominal laparotomy at three weeks; the loss of appetite was alarming because, though everyone else seemed to consider him the picture of rude health, to my wife and me James was melting away. Massive chemotherapy and kindly attention eventually turned the scale, but it was two months before James stopped looking like a scarecrow.

I find that my attitude to mothers in outpatients has become more tolerant and I am less inclined to turn a deaf ear when they claim that an apparently healthy baby has lost weight or is otherwise unlike his usual self. Needless to say, my wife has not allowed me to forget how I scorned her diagnosis, and James will no doubt be taught to display his scar on any future occasion when I am feeling pleased with my clinical acumen.

* * *

We needed some extras to ensure the smooth working of our little hospital, and we could usually get permission to buy them locally. Dinner-wagons came into this category, but none of the local supply firms stocked them or had even heard of them. However, one enterprising native contractor offered to make two wagons if we supplied the plans. I made detailed drawings of a dream dinner-wagon and suggested sheet aluminium or aluminium alloy as a suitable material. Back from the contractor came a quotation which seemed not too outrageous. The construction material was specified as "$^1/_8$ M.S.," which meant nothing to me or the supply officer who passed the specification. The order was placed and in due course we were asked to collect the first wagon. It was made of $^1/_8$ inch mild steel sheet and was in consequence as strong as an ammunition locker and quite as heavy. This was unhappily the only time in our experience when a native contractor had worked to specification.

A sweating screaming pack of coolies pushed the monstrosity up a ramp into our truck, where it promptly fell partly through the floor. At the hospital we had

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to use a crane to deposit it outside the kitchen door. Rather hesitantly we asked Sister to come and see how she liked it. She came and admired, for it was superficially quite elegant, and then vainly tried to lift the cover from the food trays. It was so heavy that she could not even budge it, but as we had plenty of helpers this did not seem an insuperable difficulty. The wagon was pressed into use; but a few days of trundling its massive bulk along the verandahs was enough to plough up the thin sandy concrete of which they were built. Finally one of the inadequate wheels fell off and the wagon listed majestically over. It was pulled level by main force, and, supported by a brick, served thereafter as a static—a very static—serving-out counter. For all I know it may still be there, a monument to the solidity of the British Raj.

* * *

The old man wiped the froth off his face with the back of his hand. "Her's gorn in agen," he said mournfully but with some pride. "Where?" I said. "Gaol o' course" he said eyeing me suspiciously; then, apparently reassured, "always does for the winter; rare spirit her has. Seventy-six convictions when I wed her, turned 70 then, her was." "Why did you wed?" I asked. "Well rightly I didn't have much to do with it, it was the W.V.S. and they welfare workers done it. 'Twas worth it though; they give me a big breakfast, a room looking onto a garden, and a ride in a motor-car. You'd have done the same." I agreed. "They thought I'd keep her out I s'pose, but 'tis no good, if her's made up her mind, then in her goes." We sipped our beer in silence. "Yes, only last Friday her said 'Winter's acoming Charlie', her said, 'and it's getting too cold in the shelters for my old bones, so I'm agoing in agen.' 'Alright my love,' I said, 'I'll acome up with you'; so we went up to the Police, and her stood outside and her swore. After a minute two sergeants come out and take her in. Then they throws her out agen. Then her swore proper. Some fine spirit her has. Then they come out agen and take her in and charge her, and I knowed her was comfortable for the Winter. Went to court Monday, when her came up before the beak. Her opted for B—— gaol; it's warmer in there."

* * *

NOW YOU'RE HERE

Now you're here, Doctor dear, when you've looked at Uncle's leg,
Will you come and see an Orpington in trouble with an egg?
Will you look at Rupert's tonsils and advise about the cat?
Then I'll take you to the cesspit, you must have a peep at that.
The Sanitary Person saw it last in '41
And assured us it was *urgent* and that something would be done.
Well, nothing *was*, of course—but just a teeny word from you
To the rural district council and what wonders that would do!
Oh, by the by, please certify that Claud is fit for camp
Before you see the cottage which is letting in the damp.
I can't believe it's healthy there, though Mrs. Postlethwaite
Has spent her life in it, she says, and now she's 88
And never has an *ache* (except the usual catarrh)
How *illness-proof*, it seems, the older generation are!
Do *you* think Jane should marry that *peculiar* young man?
If those whiskers will not warn her, you're the only one who can.
If you can't reintroduce *her* to the straight and narrow path,
Introduce *him* to a razor or, at any rate, a bath.
May I offer you some coffee or perhaps a glass of beer
Now you're here?

Where's he gone? How very queer!
I was talking to him—here . . .
But how *could* he disappear . . . ?
Can that be him changing gear?
Yes it is. Oh dear, oh dear.

Letters to the Editor

TOXIC EFFECTS OF TRIDIONE

SIR,—In their article of Jan. 8 Dr. Briggs and Dr. Emery report that of 10 patients with petit mal who were treated with 'Tridione,' 7 were improved, but that 2 of these displayed serious toxic effects, with death of 1. The authors conclude that "in this short series the toxic complications of tridione proved more dangerous than the disease it is used to treat." A reader of the case-reports cannot but wonder whether the medicine or the manner of administering it was more at fault.

In case 9, after neutrophils had fallen to 2000 per c.mm. medication was nevertheless continued for two months, presumably without blood examination. The neutrophil count after that time was only 700 per c.mm. Tridione was then discontinued, but in spite of the fact that the neutrophil count "fell steadily," no active treatment was instituted until five weeks later when the neutrophils had fallen to 100 per c.mm., and there was severe depression of all elements of the bone-marrow. A single transfusion of a quart of fresh blood was then given and fortunately the child eventually recovered.

In case 10 the child developed nephrosis, caused, the authors believed, by tridione; yet this medicine was continued during the last five of the eight months that the child lived.

Like many other potent drugs, tridione must be carefully supervised and medication stopped promptly if symptoms of serious toxicity appear. The danger is increased if the anticonvulsant, methylphenylethyl hydantoin ('Mesantoin'), is given coincidentally. During the past four years, we have given tridione, or its analogue, 'Paradione,' to nearly 300 patients with epilepsy. One death from aplastic anæmia, the first encountered anywhere, occurred early in the series. Since the institution of monthly blood examinations and prompt cessation of medication when neutrophils fall below 1600 per c.mm., no serious blood complications have ensued. In some patients medication has had to be interrupted a number of times. One other patient displayed evidence of nephrosis; medicine was stopped promptly, and neither kidney symptoms nor petit mal have returned. In compensation for these two instances of serious toxicity, the great majority of patients with petit mal (pyknolepsy) are greatly improved. The saving in petit mal for this single group of patients amounts to something like 300,000 a year. Like any potent weapon of offence, tridione can cause grave harm if not handled with respect and conscientious care, but this would seem to be a poor reason for not using it.

WILLIAM G. LENNOX.

Neurological Institute, Children's Medical Center, Boston, Mass.

SANATORIUM NURSING

SIR,—Dr. F. J. Bentley, in his article of May 8, suggested that we should adopt in British institutions the less rigid régime of bed rest which he observed when visiting Swiss sanatoria. In this way, he thinks, the depressing outlook for patients awaiting admission to sanatoria, where wards have been closed because of the shortage of nurses, might be alleviated. Correspondence on his article indicated the interest it aroused. May I, as a sanatorium matron, be allowed to add a few comments?

In the thoracic surgery unit of a sanatorium as many nurses will always be required as in the surgical ward of a busy general hospital; but in the ordinary sanatorium wards it would be possible almost to halve the numbers of nurses at present employed, if the long rounds of bed-pannings, bed-washings, and bed-makings could be cut by half. Sanatorium doctors in this country are rightly reluctant to make any move towards lowering the standards of nursing; but if, after weighing all the evidence, they could satisfy themselves that gentle walks to the ward washrooms and sanitary annexes would involve the expenditure of no more energy than the straining on bed-pans and washing in bed; that a patient making his own bed, slowly taking his own time to do it (especially where the spring mattress which does not have to be turned is provided) is tiring himself less than

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when he sits up for an hour to work at occupational therapy—then changes likely to alter the staffing outlook completely would be at hand!

Constant filling of hot-water bottles in the winter takes up many sanatorium nurse-hours. Is it likely that electric heaters will ever come into use? In sanatoria built in the pavilion style, the provision of a central office into which bells from every bedside would ring, might perhaps make it possible for a night sister (doing frequent rounds and having two "runner" nurses at her disposal) to give as good attention at night as five or six nurses do under the present system where a nurse must sit throughout the night in every ward.

MARIE A. SIMPSON.

ESTIMATION OF BASAL METABOLIC RATE

SIR,—Your correspondents Miss Lovell and Dr. Martin (Feb. 12) are not quite fair to Dr. Bene. If their figures be tabulated in broad classes we obtain:

Basal metabolic rate	R.P. index <900	900–1300	1300–1700	1700+
> +45	..	2 *	5	8
+25 to +45	..	2	4	2
+ 5 to +25	1	8	1	..
< +5	6	3	4 *	3 *

Of the 49 results which are all I can find in the scatter-diagram, 9 show gross lack of correlation between the basal metabolic rate and the R.P. index; I have marked these with an asterisk. Dr. Bene claims a good correspondence of results in about two-thirds of cases; I submit that this claim is supported by the figures of Miss Lovell and Dr. Martin.

I cannot help wondering whether Miss Lovell and Dr. Martin are not getting somewhat high basal metabolic-rate results. A respiration-rate of 18 per min. and a pulse-rate of 64 per min. give an R.P. index of 1150; according to the scatter-diagram, in most cases this would be associated with a basal metabolic rate of at least + 20.

Sheffield. ARTHUR JORDAN.

CONSCIOUSNESS AND ITS DISTURBANCES

SIR,—Psychiatrists will be grateful to Dr. Purdon Martin for his lucid exposition of current knowledge of the cortical and hypothalamic foundations of consciousness (Lumleian lectures, *Lancet*, Jan. 1 and 8). Some, however, will find something to ponder over in his statement that "it is generally agreed that we cannot detect any awareness of mental processes; all awareness of self seems to be bodily." The terminology here used is open to misunderstanding unless it is clearly understood that the same processes which, on the one hand, can be registered as biological epiphenomena of nervous activity (objective consciousness), can, on the other hand, also be seen in the light of psychology (subjective consciousness). In subsequent passages Dr. Purdon Martin does, indeed, more justice to these dual aspects by introducing subjective self-awareness, which, he argues, may be based on a "body-and-mind image" analogous to the body-image so important for objective consciousness.

As regards the awareness of mental processes, it is true that we are never aware of their activation on the biological (neuro-associative) level. It has, however, been shown by a certain school of experimental psychology [1] that we can reflect upon the formal characteristics (apart from the contents) of mental processes, not concurrently but immediately after we have performed them (e.g., on how we have reached a conclusion or on how we have formed a new concept). Mental processes are too often thought of as atomistic and momentary, whereas they can be embodied into dynamic wholes extending over a period of time, as in a mental conflict when we may be aware of its various phases. Even in "dream work," which is going on while the awareness of the body-self is relatively dormant, there can be full recollective awareness of formal features as well as of contents extending over a sequence of scenes. The great bearing which problems of self-awareness have on psychopathology and psychotherapy need hardly be stressed.

Sedgefield, co. Durham. STEPHEN KRAUSS.

1. Kuelpe, O. Report of Congress of Experimental Psychology, 1904. Ach, N. On Volitional Activity and Thinking. 1905. Buehler, K. Facts and Problems of a Psychology of Thinking, *Arch. Psychol.* 1907, 9. Titchener, E. B. Lectures on the Experimental Psychology of Thought-Processes. New York, 1909. Selz, O. The Laws of Ordered Thinking. 1913.

COLDS

SIR,—Colds do not affect those who live and sleep in the open air, children kept in open-air schools, or patients living and sleeping in the open air; while nurses who attend them and occupy warmed rooms suffer. Soldiers in trenches suffered colds only when coming home on leave; lumberers, working in arctic cold, had pneumonia only when given a warmed hut to sleep in; arctic travellers marooned on an ice-floe for weeks and exposed to the greatest cold were free from illness such as is attributed to exposure to cold in the popular mind.

In *Open Air and Sunshine* (London, 1924) I dealt at length with the great protective effect of cold air on the respiratory membrane. Such air, even if misty, when heated up to nearly body-temperature in the breathing passages, becomes relatively dry; and taking up much moisture, evaporated from their membranes, is expired almost saturated with water vapour at that temperature to which it is warmed. This means much blood flowing through the capillaries of the membranes, and secretion by these. Comparing a crowded room at 72°F, and almost saturated with moisture, with open air at 40°F, the evaporation will be in the whole day about 200 g. of water in the former and about 350 g. in the latter case.

The increased breathing produced by much active exercise may double this output, and heat-loss from the membranes may become nearly 4 times greater in the open air, and the evaporation 3½ times greater. The mucous membranes are then far more thoroughly swept with arterial blood and washed with secretion, and so defended from infection, which in its turn is minimal out of doors. The dusty air in rooms may also be of evil influence in the cleansing of the membranes by the ciliated epithelium. In the cold wind the eyes water and the nose runs, through the enhancement of secretion, to keep the membranes at near body-temperature. In the case of air saturated at 85°F, as might be in a very crowded warm room, the evaporative and heat losses might be 10 times less than in the open air.

Workers in chemical factories where there is escape of a small quantity of an irritant, such as sulphur dioxide, are reported to be relatively free from colds; so too snuff-takers. The Victorian habit of using smelling-salts may have been of benefit by exciting secretion. In the summer people are far more in the open air, and return from holidays to stuffy heated railway carriages, and rooms where infection is spread. Thus colds become prevalent when wintry weather begins.

Smallfield, Surrey. LEONARD HILL.

A PUBLIC DIET RESTAURANT

SIR,—When in Prague last December, I dined at the Public Diet Restaurant. This interesting new social service is being developed by U.R.O. (the Czech T.U.C.) in conjunction with three doctors.

Two meals are served—at midday and in the evening. The restaurant is subsidised by U.R.O., so the price of the meal is halved; it is 2*s*. for the regular customer and 3–4*s*. for the casual diner. As is usual in Czechoslovakia, some ration tickets have to be given up; but the special-diet rations provided make this less of a hardship than for the average person.

A doctor's prescription is necessary to entitle one to a meal. The cooking is done, by two dietitians and two cooks, under the supervision of a doctor, who visits the restaurant daily and whose name is printed on the menu. The food is really good—well chosen and cooked, and served in style, as might be expected of a good restaurant. This attractive presentation must be doubly welcome to people faced with the deprivations and difficulties of a special diet, and bereft of the comforts of favourite foods. Still more helpful must be the restful and luxurious atmosphere of the dining-room;

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with its small tables, linen cloths, flowers, shaded lights, and skilful waiters.

Five diets are served—gastric, salt-free, low-fat, nephritic, and diabetic in three standard groups (150, 200, and 220 g. carbohydrate). Menus are table d'hôte and à la carte. I had a gastric diet—cauliflower soup (Czech soups are especially good) with egg and milk in it, a large portion of steamed carp, with melted butter and lemon, and creamed potatoes, followed by sponge-cake decorated with cream. A cup of hot rose-hip tea was served with sugar and thin slices of lemon; this is a pleasant hot drink, containing, I was told, about 9 mg. ascorbic acid to the cup. The calorie value of the meal, which was satisfying as well as attractive and digestible, was between 600 and 700.

It was pleasant to see about 300 people enjoying amenities not usually associated with public hospitals or public services. It would be interesting to try a similar experiment here in a small town or in association with a hospital kitchen.

London, W.3. P. B. FISHER.

HISTOPLASMOSIS

SIR,—I was interested in Dr. McCracken's report[1] of negative histoplasmin skin tests, to which he referred in his letter of Feb. 12. In 1947, Dr. G. W. Downes tested 100 children admitted to Guy's Hospital (ages 2 to 12 years; rural 12, urban 88). He also found no positive results with 0·1 ml. of 1/1000 histoplasmin injected intradermally.

Guy's Hospital, London, S.E.1. PHILIP EVANS.

PSYCHOLOGICAL TESTS IN THE ARMY

SIR,—My attention has been drawn to Army psychological tests by my son, a conscript, who apparently is not permitted to forget that he flunked at dominoes when he joined-up some months ago.

It is important that the democratic public should know what is going on, and so the informative account of "Psychological Tests in the Royal Navy, Army, and A.T.S.," published in *Occupational Psychology* (1947, **21**, 53), is very welcome. The story—told by Mr. P. E. Vernon, PH.D., who in 1941 was appointed as a consultant on research to the psychologists at the Admiralty and the War Office—reveals a child-like faith in the tests, a faith which Podalirius would have found perturbing; and the psychologist appears as a know-all, the testee as a buffiehead.

Of abstraction tests, which provide one of the most important contributions to group-testing technique made during the war, Dr. Vernon remarks "The scoring is completely objective, i.e., there is no danger of the appearance of alternative or partially right answers." But we will take some of his examples and assay them ourselves:

(1) "*big little rough smooth hard* * * * *"
Is there not an EASY alternative to the SOFT answer which turneth away wrath?

(2) "*oz. lb. stone cwt.* * * *"
If TON is the vogue, the alternative WEY is barred, and it is not surprising that the psychologist finds the dependence of the test on verbal ability to be very low.

(3) "*luck lick lack foul foil* * * * *"
"A simple vowel-change," thinks Testee and answers FOOL. "FAIL, to you," rasps Psychologist, now a little hoarse, "the correct and *only* answer is FOAL." "F * * *," euphoniously rejoins the testy soldier, this time partially right.

(4) "*AzM bXn DvO gTp* * * *"
This may be one of the "very difficult" items, and to acquire merit the testee should therefore reply *KrQ*, not just *OiC*. It is fatal to be unorthodox—to venture *LrQ* is to be outed *PdQ*. The heterodox solution, *LrQ*, however, is perfectly pukka, for to the Supreme Mathematician the sequence 1, 2, 4, 7, 12, 20 and its homologue A, b, D, g, L, t are just as pure and holy as 1, 2, 4, 7, 11, 16, 22 and A, b, D, g, K, p, V.

The pyxing of tests is clearly a tricky business and the danger which Dr. Vernon believes to be non-existent is a real one. Perhaps we need a Belisha beacon.

From abstraction tests let us turn to orientation tests.

If when standing on your head you are facing East, in what direction is your right arm pointing—N, S, E, or W?

The catechizee should continue to play for safety and give the prayer-book answer, "N." All the same I have just stood on my head facing East, although—until I noticed that it was to the East that my right arm was pointing—

"I feared it might injure the brain;
But now that I'm perfectly sure I have none,
Why, I do it again and again."

Perhaps these few examples, all taken from Dr. Vernon's paper, will serve to show how very thin is some of the ice upon which the psychologist skates so sweepingly. "For the same subtlety of the subject," observed Bacon, "doth cause large possibility and easy failing; and therefore the inquiry ought to be the more exact."

PATER.

HOSPITAL PHARMACISTS

SIR,—Hospital pharmacists all over the country are up in arms against the functional Whitley council set up by the Minister of Health. Deadlock has been reached.

Opticians, who may qualify in six months or even by a correspondence course, receive £500 a year after two years' experience, and rise to £800: one in four can then go on to £900–£1200. On the other hand, at the age of 65 only 85% of hospital pharmacists can be sure of £600; and they have five years' training, often at a university. Responsibilities, moreover, have increased as the real value of their salaries has dwindled.

An efficient hospital service necessitates many skilled professional personnel in addition to medical and nursing staff. For such people a sense of vocation cannot be expected to suffice; salaries must be commensurate with responsibilities and cost of training. Inadequate remuneration has produced a shortage of nurses and a dearth of recruits. Cannot the Ministry see that a similar policy is bound to produce the same result with these professions? Even now the hospitals are calling out in vain for men and women of skill.

London, W.9. ARTHUR G. SHAW.

SPLENECTOMY IN KALA-AZAR

SIR,—The paper by Air Vice-Marshal Morton and Flight-Lieutenant Cooke in your issue of Dec. 11 raises a number of important points.

First, it is difficult to see how removal of the spleen alone can have any marked effect on this disease which involves the whole reticulo-endothelial system and is not limited to one organ.

In the series of patients submitted to this heroic procedure, sternal puncture was positive in only one; yet in the negative cases *Leishmania donovani* was found in all the sternal smears. It is most regrettable that of late years, particularly in the Services, splenic puncture has fallen into disrepute, while sternal puncture is looked upon with undue favour. Those of us who worked in kala-azar areas before the late war have seen few, if any, casualties from splenic puncture; and the diagnostic value has been infinitely higher. This view is still held in the mission hospitals in Bengal.

From the point of view of treatment I note that only one patient had received 'Urea stibamine.' During the late war I saw a number of so-called antimony-resistant cases of kala-azar which had been treated with the more modern pentavalent antimony compounds without success; and every one of these cleared up dramatically with intravenous injections of urea stibamine. Two patients, I remember, were on the point of having their spleens removed on the assumption that they must have Banti's disease. In my small experience of the so-called refractory Sudanese kala-azars, I considered that intravenous urea stibamine would probably have resulted in cure in those cases which had failed to respond to other antimony compounds and were being successfully treated with stilbamidine.

I agree that negative marrow-smears are insufficient to exclude the diagnosis of kala-azar, but I consider that a splenic or liver puncture is essential. Possibly splenectomy should be considered after proof of drug

1. McCracken, B. H. *Thorax*, 1948, **3**, 45.

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resistance, but I would only call a case resistant after repeated courses of intravenous urea stibamine and lack of response to stilbamidine; and I have seen no case that would not respond to one or other of these lines of therapy.

Nelson, New Zealand. R. L. HAVILAND MINCHIN.

LIVER EXTRACTS

SIR,—I have followed with great interest the discussion in your columns initiated by Dr. McSorley with his letter of Jan. 22. In Norway our experience is similar, though here the difference between single batches is not so great, as we still are fortunate enough to have access to fresh frozen calf-liver as a starting-material.

As I have pointed out,[1] the sort of liver from which the extracts are prepared is important—a fact underlined in experiments by Laland and myself (unpublished) with extracts made from pigs' livers by a method based on that of Laland and Klem.[2] For three years in succession we have observed that hog-liver gave active extracts only during the summer and autumn months, while liver from pigs given "winter food" was inactive or pretty nearly so. Whether the same is true also of liver derived from other animals I do not know; at least the phenomenon has never been observed with calf-liver—our usual raw material.

Experience in this country (Thjøtta and Jonson, personal communication) with *Lactobacillus lactis* Dorner as a means of assaying anti-pernicious-anæmia potency is akin to that reported by Dr. Shaw (Feb. 5).

University of Oslo. JENS DEDICHEN.

GUM-SALINE

SIR,—During the 1914–18 war Bayliss introduced the use of 6% gum-acacia in normal saline as a fluid for intravenous use in the treatment of shock and hæmorrhage; and by the end of that war the clinical efficacy, the safety, and the convenience of the fluid were proved. Thereafter gum-saline was widely administered, and, in common with many other clinicians who have used it extensively, I have no doubt about its efficacy in restoring blood-volume or about its freedom from serious drawbacks.

Early in the late war plasma was introduced as a fluid to restore blood-volume; and for a number of reasons gum-saline was soon forgotten, though never found unsatisfactory. I have always regretted the popular change from gum-saline to plasma: firstly because I have never seen any clinical evidence that gum-saline is less effective than plasma in rapidly restoring and maintaining blood-volume; secondly because from experience I have come to regard gum-saline as safe; and thirdly because on theoretical grounds the potentialities of undesirable (though as yet unknown) results from the use of protein intravenously are vastly greater than those from the use of simpler chemical substances such as gum-acacia. Recently bottles of plasma have been supplied with a warning notice attached. The warning must be familiar to all, but the first paragraph is short enough for quotation. It runs:

> "Important. To the Doctor in Charge. Dried plasma or dried serum is thought to transmit hepatitis in up to 10% of those transfused. The disease may not manifest itself until three or more months after transfusion, and, while usually mild, may be fatal."

I am at a loss to understand how anyone can offer for human consumption a fluid with such potentialities. It is not a good enough answer to say "you have been warned." Anyone who has worked with modern intravenous-minded doctors must know that a plentiful supply of an intravenous fluid conveniently packed is sufficient invitation to ensure its use. If it is as poisonous as the label on the bottle suggests (and indeed it may be worse), it ought never to be distributed for general use.

My own remedy for the situation seemed at first sight very simple—to forbid the use of plasma in all patients for whom I had clinical responsibility, and to insist that gum-saline should be used, since I knew the latter to be both effective and safe. But I had not reckoned with one other essential—that the gum-saline should be readily available. I am now astonished to find the greatest difficulty in obtaining supplies. Well-known manufacturers of the highest repute and enterprise who used to supply gum-saline, no longer make it and appear to be unwilling to start again. One such manufacturer expressed the greatest surprise that anyone still had a use for it.

Possibly trials with new substances such as dextran may produce a fluid which is superior even to gum-saline; but in the meantime let us at least be allowed to buy what has for thirty years proved a safe, effective, and sometimes life-saving fluid.

If my letter to you, Sir, stimulates enough others to ask for gum-saline, manufacturers may be persuaded to supply it again.

London, W.1. G. F. GIBBERD.

1. C.R. 20e Congrès de Médicine Interne des Pays du Nord, Réuni à Gottenbourg du 27 au 29 Juin, 1946. Helsingfors, 1948; p. 313.
2. Laland, P., Klem, A. *Acta med. scand.* 1936, 88, 620.

MESENTERIC ADENITIS

SIR,—In connexion with Mr. Hickinbotham's letter of Feb. 5, I should like to report a case seen by me last year.

A male infant, aged 22 months, had a 3-day history typical of intussusception—the passage of blood per rectum, and quiescent periods interspersed with bouts of crying out in pain. On examination there was an indefinite, sausage-shaped tumour on the left of the abdomen, and per rectum there was blood and mucus. A paramedian exploration revealed some thin bloodstained fluid in the peritoneal cavity, the entire mesentery studded with enlarged glands typical of non-specific mesenteric adenitis, the whole length of the small bowel remarkably spastic and collapsed, and two easily reducible entero-enteric intussusceptions—one about 2 ft. from the ileocæcal valve and the other 2 ft. from the duodenojejunal flexure.

It seemed possible that these numerous glands were irritating the autonomic nerves in the mesentery, thus producing a spastic condition of the bowel and painful self-reducing intussusceptions. It would be interesting to note the state of the mesenteric glands in cases of ileocolic intussusception.

City General Hospital, Stoke-on-Trent. F. V. A. BOSC.

DENTAL CONDITIONS IN PULMONARY TUBERCULOSIS

SIR,—Correlation of dental conditions with systemic disease is a field which has often been neglected. We would like to stress the possibilities of closer coöperation between the chest physician and dental surgeon in the assessment and treatment of pulmonary tuberculosis.

In 1937 the Borough of Southwark opened a dental clinic in the tuberculosis dispensary, and as a result the chest physician and the dental surgeon, each of whom was interested in the other's work, were able to make parallel observations on the oral condition and the progress of the lung disease. It soon became apparent that dental caries was frequently seen in association with active tuberculosis even during the immune period (25–40). After further observations it was found possible to divide our findings into six main groups:

1. Active caries in newly diagnosed cases with active lung disease.
2. Active caries in treated cases which have become quiescent, coinciding with reactivation of the lung disease.
3. Active caries with evidence of old paradental disease in new cases with evidence of widespread lung damage and relatively recent symptoms.
4. Paradental disease in a new case coinciding with widespread pulmonary disease with very few symptoms.
5. Paradental disease in treated cases of long standing showing a marked tendency to chronicity or arrest.
6. The gradual onset of paradental symptoms with quiescence of the dental caries as the active lung lesion becomes controlled. This is particularly noticeable in cases treated by collapse therapy.

Thus it will be seen that we have in a well-informed opinion on the oral condition a useful pointer to the

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activity of the lung lesion. Particularly is this useful in the assessment of the minimal lesion. Again the onset of dental caries in an apparently quiescent case may give the chest physician the first warning of a possible relapse.

We have little doubt about the significance of our observations and we are preparing a paper to enlarge on these findings. We think this matter worthy of further research, not only to confirm the usefulness of these parallel observations but also to explore the causative mechanism. In our opinion a possible field for investigation lies in the sympathetic-parasympathetic balance.

Tuberculosis Dispensary, Bermondsey and Southwark Group Hospital Management Committee, London, S.E.17.

E. K. PRITCHARD
Chest Physician.
G. E. KING-TURNER
Dental Surgeon.

AID TO ABDOMINAL PALPATION

SIR,—I was interested to read Mr. Nicholson's article, in your issue of Jan. 29, on respiration and abdominal palpation. A similar method of achieving the same result—i.e., abdominal relaxation—came my way during the war.

With the patient lying flat on the bed, the examiner places his hand on the abdomen in the usual way. The patient is asked to breathe actively with his abdomen—which he will do without difficulty if he is told to raise and lower the examiner's hand in the vertical plane by his respiratory efforts. Palpation is found to be easy when the hand is being lowered by the descending relaxing abdominal wall. I have never seen an adult patient who could not understand, and thus perform, this simple exercise, unless there was extreme involuntary rigidity.

I agree that "if the rigidity is produced by a conscious effort it will usually disappear if thoracic respiration can be restricted"; but I would add that it will also disappear if abdominal respiration be initiated by the method outlined above.

London, W.14. D. W. S. SHELDON.

INDEPENDENCE IN RESEARCH

SIR,—It is surely no accident that topics of philosophical and political interest are increasingly being discussed in the medical press. We are living in a period of change, and medicine is not immune. There is, however, a barrier of ignorance and prejudice to be broken down before such discussion can become directly useful to medicine. For example, Mr. Doran (Jan. 29) presents a picture of the relation between science and philosophy in ancient Greece that is far from being universally accepted. Plato and Socrates are said to have rejected "science" because it was not interested in man and his problems. Yet this rejection included the embryonic scientific and genuinely human approach of the Hippocratic school. Prof. Benjamin Farringdon in his Pelican *Greek Science* quotes the unknown author of the Hippocratic tract "On Ancient Medicine" as priding himself on being a worker, a craftsman, a technician. Plato rejected the theoretical achievements of such craftsmen and artisans because they were workers and their views were dangerous to the rulers of the time. He consolidated the conception of philosophy as the responsibility of members of a ruling caste freed from the need to work by dependence upon the labour of slaves. The *Republic* is an idealised picture of a slave State, and, for all the greatness of his contribution to thought, the writings of Plato were the product of a class society and have since repeatedly been used in defence of succeeding forms of class society.

Today it is impossible to unravel the complex problems involving relations between philosophy, philosophers, and practical social and scientific activity, without an appreciation of the relation between forms of society and their critics and defenders. The Lysenko controversy is an example of such a problem—a vital current controversy involving the problem of freedom and control in science. It can only be properly understood against the background of the position in the world today of the philosophic concepts underlying Lysenko's work and the support given to it by the Soviet political leaders. Lysenko takes a stand on the basis of dialectical materialism—the philosophy of communism. The issues involved cannot be evaluated without a study of Marxist dialectics, and the evaluation of Plato in relation to Hippocrates is far from irrelevant. Letters cannot provide more than skirmishing in this the most topical issue of the day in its relation to medicine. I should welcome even fuller discussion in THE LANCET of the impact of these fundamental aspects of life upon medicine.

Birmingham Accident Hospital. RUSCOE CLARKE.

INTRAVENOUS TREATMENT OF ANÆMIA WITH AN IRON-SUCROSE PREPARATION

SIR,—It was with considerable interest that I read the comment by Dr. Slack and Dr. Wilkinson (Jan. 22) on their article which you published three weeks previously.

I am engaged in general practice, and during the past year have used over 2 litres of 'Ferrivenin,' and have concluded that it is a particularly bland and reliable preparation; I agree with the summary in the paper by Slack and Wilkinson.

I have not encountered the complications mentioned by them, and attribute this mainly to the use of a very fine needle. Slack and Wilkinson appear to prefer a no. 2 'Record' needle, but a no. 19 has the following advantages: (1) it is almost painless; (2) it limits the speed of the injection to some extent; (3) it does not damage the vein, thus enabling patients to have their complete series of daily injections into the same vein; (4) the puncture in the vein is sufficiently small to be sealed at once on withdrawal of the needle, and there is no flow-back of the contents of the vein into the perivascular tissue, which might contribute to the complications mentioned.

Good illumination is very necessary. Then, if the needle becomes dislodged from the vein during the course of the injection, the skin in the region of the point of the needle can be seen to change to a slate-grey colour, and the injection can be stopped before an appreciable amount of iron solution has escaped. Under such circumstances, there is some pain of short duration and the skin remains discoloured for a week or two, but the vein can be used for further injections in the course of a few days.

Kidsgrove, Staffs. D. G. FRENCH.

RESISTANT STAPHYLOCOCCI

SIR,—In view of the interest in infections due to penicillin-resistant staphylococci and the recent articles on this subject in the *Lancet*[1] and the *British Medical Journal*[2] we thought the following case should be recorded.

A man, aged 22, was admitted to this hospital with staphylococcal septicæmia and died 26 days later. The organism isolated from the primary blood-culture was found to be 150 times more resistant to penicillin than the standard Oxford staphylococcus. The resistance was determined by Kolmer's[3] serial-dilution method, with the exception that the inoculum used was one drop of a 1 in 100 dilution of an 18–24 hour culture, as recommended by Barber.[4] The staphylococci isolated from the primary and subsequent cultures were all found to be penicillinase-producers. They were also tested for streptomycin sensitivity and found to be sensitive to the same dilution of streptomycin as the standard Oxford staphylococcus. After two injections of streptomycin (total dose 1·5 g.) the patient's temperature fell from 105 to 97°F, and the blood-cultures taken 24 hours after the commencement of this treatment were sterile; these were the only sterile cultures obtained from the case. After a further 24 hours the pyrexia recurred and the blood-cultures again yielded a growth of *Staphylococcus aureus*, which was now found to be 2500 times more resistant to streptomycin.

This rapid development of resistance to streptomycin, which is a well-established fact, seems to limit its value in chemotherapy.

Withington Hospital, Manchester.

LOIS STENT
KATHLEEN V. LODGE.

1. Leading article, *Lancet*, 1948, i, 219. Barber, M. *Ibid*, p. 730; *Ibid*, ii, 641.
2. Annotation, *Brit. med. J.* Jan. 8, p. 64. Barber, M. *Ibid*, Jan. 22, p. 151.
3. Kolmer, J. A. Penicillin Therapy. New York, 1945; p. 77.
4. Barber, M. *J. Path. Bact.* 1947, 59, 373.

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THE RESEARCH-WORKER'S SALARY

SIR,—Surely the Association of Scientific Workers [1] is misguided in suggesting that medical research-workers should receive a salary 10 % below that of other specialists. Is the future discoverer of the cause or cure of cancer of smaller value to the community than a tenth-rate clinician? Must he await publication of his successful researches before seeking a civil-list pension? How many clinicians would care to subject their life work to the "hurly-burly" of critical discussion by a congress of medical scientists?

I was once a full-time research-worker but lacked the patience, perseverance, and single-mindedness of my more gifted colleagues. It was also made quite clear to me that a desire to draw a salary comparable to the earnings of a mediocre general practitioner was regarded by my betters as incompatible with a desire to extend the frontiers of medicine. I have since sought and found success in another branch of our profession. May I nevertheless put forward a plea for a more enlightened view of the research-worker's reward so that a research career may attract the best intellects of the profession?

In the past full-time research has too often been the privilege of those with private means, of confirmed bachelors, and of eccentric idealists whose concern for the welfare of their families has been subdued by a child-like curiosity into the musteries of our calling.

CALDUS.

CRASH HELMETS

SIR,—The enforced use of crash helmets by motor-cyclists, proposed by Mr. Bertwistle in his letter of Jan. 22, would, I suggest, be against their best interests. Greater road safety will not be attained by any such compulsion. I consider that if all motor-cyclists wore crash helmets the accident-rate would be increased because (1) they are prone to give a false sense of security; (2) they cause headache over a journey longer than 30 miles, thus tending to impair road judgment; and (3) motor-cycling would soon be looked upon as a hazard and not as a sport and cheap form of transport.

Of course the years between 16 and 25 can be considered the dangerous age; but if riders are to be kept in cotton-wool until they are past that age I question whether their use to society in general will be as great as Mr. Bertwistle thinks.

There are unfortunately many road-users who are psychologically unsuited for driving any vehicle, although many have passed the examination and know the code-book by heart. To some of these motor-cycling appears to have a special appeal; they show this by opening the throttle wide and listening to the hard crackle of the exhaust as if it were a passage from a musical symphony, whereas it is an expression of a very, very primitive urge.

Birmingham. A. S. WARBURTON.

NEW SURGICAL AND GYNÆCOLOGICAL FILMS

SIR,—Mr. Sayle Creer has stated admirably the position of colour in film-making; on his analysis it is easy to see that the unsharpness in the cross-infection films was due to flat lighting, and in the gynæcological films to the use of the lens at too wide an aperture.

I think also that the views of Mr. Creer and yourselves are easily reconciled. I take it, Sir, that you have a wider experience of seeing theatrical films than of educational, and in that context your opinion is correct. The black-and-white films in the cinema are always considerably sharper than the colour ones; this is demonstrable by measurement and is also perceived subjectively (we have Laurence Olivier's opinion to support us here, for he is reported as saying that he chose to film *Hamlet* in monochrome because he wanted even the broad long shots which he visualised to be sharp); but on 16-mm. film, such as most educational films are made on today, the sharpness obtainable is nearly equal in monochrome and in colour. The comparison is made even closer in that most 16-mm. projectors are still fitted with lenses of so poor a quality that they are incapable of reproducing the image in full sharpness. Lack of adequate blackout in many lecture-rooms further blurs the apparent screen sharpness, for the "clear-cut" appearance of the projected image is visually dependent not only on measurable sharpness of the boundary between two tones of the image, but also on the contrast between them. It is here that colour film often gains in medical recording, for while the two films are approximately equal in image sharpness, the colour film is often capable of yielding a colour-contrast where the monochrome can scarcely distinguish any tone-contrast. So in 16-mm. work the colour film can usually appear to be as sharp as, and often sharper than, monochrome.

London, W.1. BRIAN STANFORD.

1. See *Lancet*, Jan. 22, p. 154.

MANCHESTER REGISTRARS' GROUP

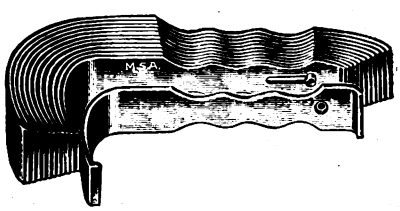
SIR,—May we, through the courtesy of your columns, announce the formation of a Registrars' group in this area, and invite those interested to contact the secretary? The Interim Committee would be interested to hear from similar groups in other areas.

8A, Rutland Drive, Kersal, Salford, 7. JAMES SHARP
Secretary, Interim Committee.

NESTED RETRACTORS

SIR,—In my Bradshaw lecture in 1947 I described a set of nested retractors. The ones I was then using were a home-made set made before the war by my chauffeur.

Since the lecture I have been working out the design with Dr. E. R. G. Greville, of the Medical Supply Association, and have, I think, got as satisfactory a pattern as it is possible to get within the limits of compactness. I and my colleagues at Guy's Hospital find these retractors very useful for all operations at the bottom of a deep cavity, such as abdominoperineal resection of the rectum, nephrectomy, vagotomy, and all operations on the œsophagus and cardiac end of the stomach, and operations on the thoracic and lumbar sympathetic systems.



The set, illustrated here, consists of twelve retractors of similar curve but varying length, held together for sterilising, and till they are needed, by a folding bolt.

London, W.1. HENEAGE OGILVIE.

STREPTOMYCIN IN WHOOPING-COUGH

SIR,—The interesting article in the Jan. 29 issue by Dr. Schwabacher and her colleagues prompts me to report a case I treated in the County Hospital, Castlebar, last November.

The patient, a young, poorly nourished boy of 9 years, was admitted with a history of severe whooping-cough and bronchopneumonia. The paroxysmal stage had lasted three to four days. He was deeply cyanosed, with a temperature of 102°F and a pulse-rate of 110 per min. A right lower-lobe pneumonia was discovered clinically and confirmed radiologically.

Treatment with oral 'Sulphamezathine' and parenteral penicillin was commenced, the latter being continued for six days with frequent inhalations of oxygen through a B.L.B. mask. The paroxysms of whooping were very severe and distressing, and numbered about 12–14 in the twenty-four hours. The condition remained stationary with no evidence of improvement in the cyanosis, temperature, or number of paroxysms. Repeated X-ray examination revealed no further extension of the pneumonia, but complete absence of any evidence of resolution.

At this stage the possibility of a *Hæmophilus pertussis* pneumonia was considered, and streptomycin 0·1 g. four-hourly was injected intramuscularly. Within forty-eight hours there was marked improvement in the general condition, the temperature became normal, the cyanosis improved, and the number of paroxysms was greatly diminished. This treatment was continued for four days, at the end of which period the number of paroxysms was reduced to about 4–6 daily, and

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radiologically the pneumonia was almost completely resolved. The patient made a rapid and complete recovery.

The pneumonia in this case was caused by an organism insensitive to the sulpha drugs and penicillin; it was reasonable to assume that this organism was the *Hæmophilus pertussis*. Following administration of streptomycin a marked improvement was noted in the whooping-cough, and the pneumonia was eased. The dosage of streptomycin was considerably larger than that used in the series reported by Dr. Schwabacher and her associates.

Galway. D. T. O'DRISCOLL.

CEREBRAL ABSCESS IN AN INFANT

SIR,—In his interesting description of cerebral abscess in an infant (Feb. 12), Mr. Farley states that a non-infective intracranial lesion would not account for 400 white blood-cells per c.mm. in the cerebrospinal fluid.

In fact far higher cell-counts have been met with in the absence of infection. I have seen a child with a spongioblastoma multiforme involving the basal ganglia who had an initial count of 540 cells per c.mm. in the fluid, of which 92% were polymorphs. Merritt [1] reported two cases of brain tumour with more than 1000 cells per c.mm. and quoted other reports of pronounced pleocytosis; the aseptic meningeal reaction in these cases is a response to a focus of necrosis near the ventricle. It is also occasionally found following a suitably placed cerebral hæmorrhage or thrombosis.

Grays, Essex. R. N. HERSON.

A NEW HEARING-AID

SIR,—Your issue of Feb. 12 contains a report (p. 289) on the 'Bonochord Duo-Minipak.' This instrument is manufactured by Allen & Hanburys (Acoustic Aids) Ltd. and not, as stated, by Messrs. John Bell & Croyden. The report says that "apart from being convertible into the duo-pack type it has no special features," thus omitting to mention that (1) the instrument can be operated either on magnetic or crystal receiver, both of the miniature insert type, (2) that a three-position tone control is fitted, and (3) that the instrument provides automatic volume limiting and background suppression.

In regard to the comparative test, no information is given on whether the 'Medresco' with a large disc and 45 volt H.T. battery, or the crystal equivalent with 33 volt H.T. was used. As the report reads, the comparison is unfavourable, and it is therefore essential to know the conditions of the test. For example, if the comparison was carried out on the basis of the duo-minipak as a one-piece aid, with only $22\frac{1}{2}$ volt H.T., then clearly the comparison is an excellent one, since the lowest H.T. battery employed on the medresco to our knowledge is 33 volt.

Bethnal Green, London, E.2. ALLEN & HANBURYS LTD.

*** We much regret our error in attributing Messrs. Allen & Hanburys' instrument to another firm. Our comparison was between the duo-minipak and the medresco crystal equivalent with 30 volts. With its H.T. battery of higher voltage, the medresco was slightly more powerful, though we considered the efficiency of the two instruments approximately the same. The provision of automatic volume limiting and background suppression is a useful feature of the duo-minipak to which we might well have drawn attention.—ED. L.

HANDOUTS FOR PATIENTS

SIR,—Readers of your annotation of Feb. 12 may like to know that the Central Council for Health Education called a conference on Nov. 4 last year to consider the production of leaflets dealing with specific diseases or specific aspects of care and aftercare, to be handed out by doctors (or on their authority by medical auxiliaries) in support of the advice given by them verbally to patients. It was felt that leaflets of this kind would reduce the possibility of the patient's misunderstanding or forgetting instructions given by his doctor.

The conference, over which Dr. E. K. Macdonald presided, was attended by representatives of the three Royal Colleges, the British Medical Association, and the Society of Medical Officers of Health. It was agreed that leaflets of this kind would be of value; and these are therefore being prepared on the following subjects: care of the aged, care after hernia operation, rheumatoid arthritis, and postnatal care of the mother. Leaflets on the following subjects are under consideration: chronic dyspepsia, chronic bronchitis, diseases of the heart, scarlet fever, postural defects, poliomyelitis, and asthma.

The conference, which is to meet again on March 3, would appreciate suggestions concerning additional subjects, or the approach that should be made and the points stressed in the leaflets.

ROBERT SUTHERLAND
Medical Adviser and Secretary.
Central Council for Health Education,
Tavistock House, Tavistock Square, London, W.C.1.

A PICTURE SOUGHT

SIR,—I wonder whether any reader remembers a picture of some forty years ago called "The Consultation"? It showed two figures on horseback, in 18th-century dress, at a crossroads: one individual, the physician, was feeling the pulse and inspecting the tongue of a seedy-looking man. I should like to know how one might trace this picture.

8, Upper Wimpole Street, London, W.1. TERENCE EAST.

A FACULTY OF GENERAL PRACTICE?

SIR,—Has not the time arrived for such a creation? The past decade has seen the recognition officially of a surprising number of specialties in Medicine, some of obscure "ætiology" or of minor significance. Why not also the general practitioner?

In course of time the G.P. becomes a true specialist in his own domain. He gets to know a considerable proportion of many other, acknowledged, specialties—not to mention law, economics, and so on. His *total* knowledge of medicine may be infinitely greater than a consultant's. Therefore let him also be enabled to put a few more letters after his name. A G.P. of 5 years' standing might become, say, an associate, of 10 years' a member, and of 20 a fellow of a College or a Faculty of General Practice.

F.F.G.P. (ANTICIPATORY).

STRANGULATED SIGMOIDORECTAL INTUSSUSCEPTION

SIR,—The following case-history shows the quite astonishing resistance of the African to physical trauma, in contrast with his lamentable lack of resistance to any kind of humiliation or mental pain.

An old African, whose age might have been anything between 60 and 80, appeared at the hospital with a mass of prolapsed bowel, rather larger than the size of a baby's head, hanging down between his buttocks. He lived about twenty miles away, far off in the bush, and he had walked to the hospital. He had had the lump for 9 days and had tried the local native remedies without success. He had been vomiting frequently for 3 days; he had eaten nothing for a week and was very thin.

The pulse-rate was 130 per min. The mass of prolapsed bowel was rubbery and soggy; the rectal mucosa was partly covered with a white slough and parts of it had become gangrenous. It smelt most offensive. The opening into the bowel was very small and difficult to find, and would not admit the little finger; it gave off a scanty mucoid discharge. The area round the opening was dark red and indurated.

It was obviously impossible to reduce the bowel, so an incision was made through the prolapsed rectal wall near the anal verge. Inside was a mass of tangled, gangrenous sigmoid. The first part of the sigmoid was, however, viable. The whole mass was lopped off, the viable part of the sigmoid being divided between clamps. A gaping hole was left with the clamped end of the sigmoid hanging out, encircled by cut rectal wall. The end of the sigmoid was closed and returned to the peritoneal cavity. The cut edges of the rectum were sewn together and pushed up out of sight. Then a left gridiron incision was made in the left iliac fossa and the end of the sigmoid was brought to the surface as a permanent left inguinal colostomy. The patient made an uneventful recovery. The rectum healed by first intention and the colostomy

1. Merritt, H. H. *Arch. Neurol. Psychiat.* 1935, **34**, 1175.

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worked well. After a fortnight he was out of danger and in 2 months he was fit for discharge.

Unfortunately the prospect of returning to the bush disturbed him. The functions of the colostomy obviously disgusted and humiliated him; he wondered what his family would think of it and the thought of returning home to them obviously worried him deeply. He began to grumble and refused to eat. He made up his mind to die and was dead in a fortnight.

My thanks are due to the Director of Medical Services, Tanganyika Territory, for permission to publish this case.

Government Hospital, Morogoro, Tanganyika Territory. C. G. F. SMARTT.

MYASTHENIA GRAVIS

SIR,—The "Disabilities" article of Jan. 29 by a patient with myasthenia gravis discloses points of considerable interest. The use of neostigmine bromide by injection, I believe, has never been reported before in the literature on myasthenia gravis, the soluble type of the drug being in the form of methylsulphate. The author reports taking subcutaneously, apparently unfiltered, a mixture of neostigmine bromide, the "binder" used to make the tablets, plus atropine sulphate, every two hours during the day and a number of times at night, probably averaging 8–10 injections in twenty-four hours. I know of no other patient who has taken daily injections over such a long period. In my experience with more than 250 patients, many observed over five or more years, none take all their medicine parenterally. The only time that injections are used by most patients is in supplement to a regular oral dosage, as a "booster" before meals when dysarthria is prominent. The tablets of neostigmine bromide may be either swallowed or dissolved under the tongue. It is most unusual in my experience, moreover, for a patient who has taken neostigmine for many years to need atropine to offset the untoward stimulation of the parasympathetic nervous system which is frequently present in the early stages of therapy but almost always disappears after a few months of treatment.

This patient has not been thymectomised although the operation has been more extensively used in Great Britain than in any other country. She might well be an excellent candidate for this operation. Patients who have had the disease for many years and have been adequately maintained on neostigmine often respond fully as well to thymectomy as those who have had the disease only a few months. In the series of 30 patients who have undergone thymectomy since 1941 at the Massachusetts General Hospital, 2, who had had the disease eleven years before operation and who had taken neostigmine for approximately half that period, are now in excellent condition nearly seven years after operation; in neither case was a thymoma found. Similar results have been obtained in other patients with symptoms of shorter duration who have taken neostigmine for a shorter time.

Myasthenia Gravis Clinic, Massachusetts General Hospital, Boston. HENRY R. VIETS.

Public Health

Influenza

THE number of deaths from influenza in the 126 great towns in the week ended Feb. 12 was 94, compared with 64 in the previous week. This figure is higher than that for the corresponding week of 1938, 1942, 1944, and 1948, but lower than that for the corresponding week of 1939, 1940, 1941, 1943, 1946, and 1947. There have been no definite reports of new outbreaks, but there have been indefinite reports of a high incidence of upper-respiratory disease in certain places.

News has been received from Dr. F. M. Burnet, F.R.S., of Melbourne, that a strain of virus A recently recovered from Ocean Islands is identical with the European strain. All strains from this country and from the Continent in the first six weeks of this year have proved identical in a full investigation by the World Influenza Centre at the National Institute for Medical Research, Hampstead.

Parliament

What the Health Service Costs

ON Feb. 17 the House of Commons, sitting in committee, considered the Minister of Health's proposal that a further £52,800,000 should be voted to meet the cost of the service in England and Wales for the year ending March 31, 1949. In presenting this supplementary estimate Mr. ARTHUR BLENKINSOP, the new parliamentary secretary of the Ministry, pointed out that the original estimates were compiled seven months before the introduction of the scheme, at a time when it was impossible to tell how far the service would be used by the public and to what extent dental and other professional services would be forthcoming. Many negotiations on remuneration at that time were still in process. It had also been impossible to tell precisely what institutions would be transferred to the service.

GOING UP

Turning to the estimates themselves he pointed out that the largest additional sum required—£22,346,000—was for the hospital services. The additional £3½ million asked for under capital expenditure covered little new building, but such items as enlarging special departments, reopening closed wards, extending nurses' homes, and repairing war damage. Fortunately more supplies had been available than they had expected and they had been able to speed up this kind of work. Nearly £19 million was sought for the running expenses of the service. Here the estimates had been based on returns supplied by voluntary and municipal hospitals with some provision for rising costs. The war had left heavy arrears of running repairs and maintenance, and an extra £5 million had been spent in this way. But over half the total of the running cost was covered by salary and wage expenditure. The Whitley councils' recommendations for the pay of nurses, domestic workers, and other staff had been made after the estimates had been prepared. The pay of student nurses, for instance, had been almost doubled at a cost of £3 million a year. That, together with improvements in other nurses' pay, accounted for an extra charge of £1½ million, with a further £750,000 for domestic workers. Provision for increases to doctors and specialists in hospitals as a result of the Spens report amounted to £6 million. Mr. Blenkinsop did not deny that this might not be the end of the wage increases, for negotiations with the profession were proceeding. But these increases had already been reflected by a healthy improvement in the recruitment of nurses. We appeared to be turning the corner in staffing the profession, and during the last 12 months there had been an increase of 3000 whole-time and 6000 part-time nurses. The bulk of the £16 million asked for under "liabilities transferred to the Minister" would be recouped from the Endowment Fund.

The comparatively small increase in the amount required for medical services was partly accounted for by the speeding up of payments to doctors. An extra £500,000 had also been very properly added to the mileage fund. Members, he felt sure, would be concerned at the large increase of expenditure on the pharmaceutical, dental, and ophthalmic service. Nearly £5 million was required for the pharmaceutical service. The original estimates had been based on the old National Health Insurance scheme, under which some 50 million prescriptions were issued in a nine-month period. Provision was made for an increase to a little over double that number. In fact something like 128 million prescriptions would be issued. The cost of individual prescriptions had not greatly increased over the estimate and there was no evidence of general misuse of prescribing by the medical profession.

A further £12 million was sought for the dental service. Here again the only guide available when they were preparing the estimates was that of the National Health Insurance scheme, of which about 7% of those entitled had taken advantage. Under the present scheme that percentage had been multiplied by 3½. Some 40% of the expenditure was for dentures, which to a large extent was a non-recurring item. Another

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large increase was the £11 million for ophthalmic services. Under the N.H.I. only 5% of those entitled had made use of this provision. Under the new service up to Jan. 31 nearly 2 million pairs of spectacles had been provided. He would not say that either on the dental or ophthalmic side the Ministry were satisfied with the rates of payment, and discussions were proceeding which would no doubt assist in future periods. In conclusion he reminded members that these figures cloaked real people and, high as they are, they were proving a real contribution to the hopes of working men and women.

Mr. RALPH ASSHETON, opening for the Opposition, pointed out that it was these same ordinary men and women who had to foot the bill. It was therefore but right and proper that these estimates should be carefully examined. The Minister of Health might be a great orator, but, Mr. Assheton suggested, he was not a very great administrator. No satisfactory explanation had been offered for his childish underestimation. Mr. Assheton was anxious lest rising expenditure might imperil the whole scheme. When the Bill was introduced the cost was put at £95 million. Last spring the original estimate rose to £132 million, and now an additional £52 million was sought. And these estimates only covered nine months and did not include Scotland. For a whole year for both kingdoms we should probably have to foot a bill for about £277 million. Nor had any great provision been made for capital expenditure, much of which would have to come in the future.

Turning to the general-practitioner estimate Mr. Assheton said it was clear that the amount spent on one or two services alone this year exceeded the total amount spent on family doctoring. Did not this show a lack of proportion? He thought that doctors were overworked and had not sufficient time for urgent cases. In country districts many doctors had been badly hit financially, while they had the mortification of seeing enormous extravagance around them. The fees paid to the dentists had wrecked the school dental service. The service was free to the individual but, he ended, it placed an enormous burden on every taxpayer and some means must be found of instilling a sense of responsibility in both those who used and those who administered it.

ACCORDING TO NEED?

Mr. FREDERICK MESSER said that anyone with experience of hospital administration would realise what a task the Minister and his advisers had faced in getting adequate estimates of cost. If these supplementary estimates showed anything, they showed the great need there was for the service. Were the Opposition criticising the machinery of getting out the estimate or did they feel that the estimate, having been made, should be maintained irrespective of its consequence? He saw in the attack the possibility of a demand that there should be a global sum of money which the Minister would be permitted to expend irrespective of the need. In his view that would be wrong.

Sir HUGH LUCAS-TOOTH felt that, if there had been an honest attempt to estimate the cost, some of the figures would have overshot the mark instead of all being below. The Minister was guilty not only of bad estimating, but of reckless understatement. Miss ALICE BACON thought that, besides underestimating the needs of the people, we had underestimated the popularity of the service. Colonel M. STODDART-SCOTT declared that doctors had never worked so long, done so much work, and filled in so many forms for so little pay.

Mr. HUGH LINSTEAD pointed out that the Minister himself had found it necessary to cut substantially the capital estimates put up by the regions for next year. The real reasons why the supplementary estimates were so high was that for six months there had been no control on expenditure by hospitals. Human nature being what it was, after ten years of shortages the hospitals had spent money freely. Hard bargains had also been struck with the Minister by the doctors and dentists, and possibly the other professions. If the Minister was to get the service on its feet he had to give way when in other circumstances he might have negotiated more toughly. There was no need to taunt the service with bureaucracy. In any great organisation there were defects which seemed to be inevitably part of its size. The Minister was trying to coördinate and at the same time to liberate the service from some of its old handicaps. There was danger that fresh congestion would result. For instance we were faced with the difficulty of the extent to which we must decentralise and at the same time standardise in the interest of a balanced service. Mr. Linstead also doubted whether the secretaryships of the boards and management committees were carrying sufficient salaries to attract the right men. When we were spending millions the people who had the effective day-to-day handling of the money should be of adequate capacity.

Sir HENRY MORRIS-JONES admitted that the Minister and his department had faced the task of launching the service with great enthusiasm, great vision, and a certain amount of courage. But he felt that there was unquestionably on the administrative side waste of money, of which he quoted anonymous examples.

Dr. HADEN GUEST urged that, in considering health centres, too much emphasis was being put on buildings. What was needed was to get teams of doctors working together in whatever accommodation they could find. The difficulty was not to get doctors into buildings, but to get groups of doctors to work together. Once the team was started it would be easy to find a place where they could work. Many small old-fashioned hospitals or, in London, dispensaries for the sick poor could be used.

BALANCING OUR SOCIAL SERVICES

Mr. DAVID ECCLES pointed out that today the social services constitute an immense transfer of wealth not from one section of the population to another, but from everybody to everybody else. We should all like the need of the people to be the only criterion of the amount of money to be spent, but in point of fact we must choose whether we spent the revenue on new houses, on education, or on health services. We must balance one social service against the other. The estimates, he continued, showed that inside the health service itself the priorities were wrong. Could it be right that the general practitioner's slice of the health service should be weighted against him in comparison with the others? The estimate was proof that we were trying to go dangerously fast. It was a negation of all the appeals for restraint which the Chancellor of the Exchequer had made. Popular though the health service was, might there not be something even more popular with the people, and that was the value of their money?

Lieut.-Colonel WALTER ELLIOT also thought that the plans for the social services were becoming so large a part of the redistribution of the income of the country that it might be necessary to have some sort of unified vote under which they could be discussed as a whole. He challenged the Government to justify these estimates by showing that facilities for treatment had been greatly increased, or that the public health had been greatly improved. He was particularly concerned by the number of tuberculosis beds which were still unstaffed. The question of balance came up again when it was considered where the money was coming from. These enormous sums now fell on the people as a whole and were reflected directly in an increased cost of living.

THE ADMINISTRATION OF THE FUTURE

Mr. ANEURIN BEVAN, replying to the debate, said he had found it difficult to discover what the Opposition were complaining about. Did they suggest that it would have been all right to spend this money if it had been included in the original estimate, or did they object to spending the money at all? Did they quarrel with the arithmetic or the policy? If the contention was that the estimate represented a grave miscalculation, that had been answered by the excellent speech of the parliamentary secretary.

When the original estimate was made he was still in negotiation with practically all the professions, and the Spens Committee on specialist remuneration had not reported. It was necessary, however, to conform with the financial procedure of the House of Commons, to put in an estimate. But when a Minister was engaged in negotiations he was subject to pressure lobbies and log-rolling. It was therefore vital, if the public interest

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was to be properly protected, that the Minister should not disclose his hand. If Mr. Bevan had put into the estimates assumptions that could have formed the basis of a negotiation by these professions, he would have been helpless. All he could do was to put in figures based upon the past remuneration.

The launching of the National Health Service, he believed, had been one of the greatest pieces of civil administration in the history of civil government in peace-time. The 11,000 devoted volunteers, drawn from all parties in the State, should have been given some commendation for their selfless dedicated service in bringing this great scheme into operation.

As time went by, he agreed, it would be necessary to evolve inside the administration of the Ministry of Health, and inside the whole health service, proper principles of administration such as those referred to in the thoughtful speech of Mr. Eccles. Nobody suggested that the hospital authorities should be permitted to spend whatever they liked. But the service must be in operation for at least one year before any comparative statistics were available to show which management committee was not behaving properly.

In the hospital administration of the future, Mr. Bevan believed:

> "We shall have global budgets determined for the regional hospital boards and the management committees of hospitals . . . . Within those global budgets the management committees will have discretion to spend what they wish on this or that item of administration. If they spend more on one, they spend less on another. What would be undesirable would be if no management committee or board of governors could repair a pane of glass without first of all having the consent of the administration, because there bureaucracy would arise. What we are trying to do is to work out a system of resilient administration with as little bureaucracy as possible, with as much local self-government as possible, and yet at the same time protect the public purse against extravagant administration."

But a hospital management committee which was spending money extravagantly and yet neglecting its duty to the patients, Mr. Bevan continued, would not be permitted to continue in that course merely because it was not spending more money than the total. It would still be necessary for the central administration to protect the patient.

It had been impossible to estimate the demand for spectacles and dental treatment. The National Health Insurance statistics had not been of any use since 1939. But the burden of suffering had proved to be much heavier than they had thought. Past conditions had concealed a vast amount of inarticulate misery and pain. In so far as these figures represented relief of genuine need everybody ought to be proud of them. Only malice was news, and the vast majority of people who were really satisfied with the service never mentioned it.

Mr. Bevan pointed out that he could have emerged from this examination clear of any charges of arithmetical inexactitude, but he would have failed as an administrator. Who had suspected before July 5 last that before the end of 1948 many more practitioners would have entered the service than the Government had expected? Who would have suspected that 95% of the population would have registered with general practitioners by the end of the year? Who would have said that by now even in the most obdurate of all the professions—the dentists—they would have got 92% in? But as these people entered the service, naturally the expenditure went up. That mounting expenditure was an expression of administrative success, because if these people had not come into the service he would have had a surplus instead of a deficit, and he would have been praised by the Opposition for being a financial success and a failure as a Minister of Health.

As this great scheme unfolded itself, Mr. Bevan ended, it would be necessary for any Minister of Health to have the support of the House of Commons in seeing that the money spent on the health services was spent where it was intended that the most good should be done, and that was not upon the most articulate members of the community, who might be the doctors, dentists, chemists, ophthalmic opticians, or even the health workers. Each one of those sections was highly organised and could bring pressure to bear upon Parliament and upon Ministers. But there was only a limited amount of money to be spent at any time on all our social services, and if it was spent prodigally in one direction it was not available in another. He was anxious that the money should not be spent on persons who could organise themselves into loud pressure-lobbies, and get columns in the Press, but on the patients who had to make use of the service.

The Supplementary Estimate was agreed to without a division.

Cutting the Dentists' Earnings

In the House of Commons on Feb. 15 Mr. JOHN BAIRD moved the annulment of the amendment to the dental regulations presented by the Minister of Health on Dec. 23 in an attempt to curb the very large incomes being earned by dentists and to bring these into relation with the Spens report. Declaring his interest as a practising dental surgeon, Mr. Baird said that he was not attempting to justify the present high level of dental incomes. His criticism of the regulation was not that the Minister was making a cut but of the method by which it was being made.

The Spens Committee on dental remuneration considered that a dentist in his prime, working for 33 chair-side hours a week, should earn £1750 at present-day values. The dentist in the National Health Service, unlike the doctor, was paid by a scale of fees. When this scale was introduced in July last the Minister made it clear that it was temporary and experimental, and that it would have to be modified in the near future to bring it into line with practical experience. The proper method for cutting the dentists' income would surely have been to revise this scale of fees rather than chop down by 50% anything over £400 a month. Why should the dentist who was working wholeheartedly within the scheme, and accepting none but State patients, be penalised by this cut, when the dentist who was working in the scheme only part-time and doing no more than he need—i.e., the dentist who took up to £400 from State patients—got off scot-free?

Mr. Baird agreed that dentists' incomes must be cut, but they should be cut equally. Under this regulation the cut would vary according to the date of payment in the area in which the dentist lived. Dentists who had come into the scheme late and only because of pressure of public opinion—of whom there was a large number—would not have their incomes cut until they reached the full gross income of £4800, whereas dentists who had worked sincerely in the scheme and were owed, say, £2000, would suffer a cut after their income had reached £2400. Mr. Baird also thought that unfair anomalies would arise for dentists in regard to existing contracts and the payment of anæsthetists' fees.

Apart from these minor anomalies the cut would create a black market in dentistry. Some dentists, who were bringing the profession into disrepute, when they had done their quota refused to treat any more patients unless they agreed to be private patients. The Minister's regulation was encouraging these immoral dentists. Mr. Baird held that with good health and a well-organised surgery a dentist could work over 42 hours a week and still do a good job of work. With the present shortage of dentists and demand for treatment he should be encouraged to do so. Owing to the shortsightedness of the Minister the priority dental services had already to a great extent broken down, and if this regulation was allowed to stand without amendment the general dental services, in certain districts at least, would also break down. His criticism of the Government was that they had not gone far enough on Socialist lines. The only solution for both doctors and dentists as far as remuneration was concerned was a salaried service. To please the professions and the Opposition in Parliament the Government had introduced a compromise, and a considerable number of dentists had taken advantage of that compromise. They had misused the trust that Parliament had placed in them. If they continued to degrade their profession the Government would have no alternative to introducing a full salaried service.

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Mr. ARTHUR BLENKINSOP, parliamentary secretary to the Ministry of Health, said it had been clearly understood at the outset that the shortage of dentists precluded any effective dental service for the whole country. The service which had in fact been given had only been possible by seriously overworking many dentists. It was clear that even with these cuts the dentists were earning a great deal more than was envisaged in the original Spens report. The Minister had felt bound to take emergency action, but he was anxious to discuss the whole question of remuneration with the dental profession with the object of arriving at a solution which would be satisfactory and fair to them in the light of the Spens report, and fair to the great body of taxpayers. Any service which required longer working hours than 42 could not benefit either patients or dentists. It was 9 hours above the figure recommended by the Spens Committee. He hoped Mr. Baird would accept the assurance that the Minister was most anxious to discuss the whole field with the dentists and to arrive at a satisfactory final solution. The orders before the House were not regarded as more than emergency requirements.

Mr. Blenkinsop added that the retrospective payments on the old dental letters were under discussion; anæsthetists' fees were included in the 52% of practice expenses allowed, which he thought were quite adequate. The motion for annulment was by leave withdrawn.

Female Circumcision in the Sudan

On Feb. 18, in the debate on the adjournment, Sir BASIL NEVEN-SPENCE deplored the continuance of this barbarous custom. Miss Hills-Young in her recent report stated that practically all the girls in the Northern and Central Sudan were subjected to this form of mutilation between the ages of 4 and 10. Replying to a parliamentary question the Minister of State had lately expressed the opinion that the legislation passed in 1946, which permitted the mildest form of mutilation but made the severe form a penal offence,[1] had mitigated the practice. But this, Sir Basil held, was wishful thinking. In fact the custom was spreading in the west, where the severe form of mutilation was ousting the less severe. It had also appeared in the Nuba Mountains where it was until lately unknown, and there was evidence that it was spreading among the tribes of the south. Unwillingly he was driven to the conclusion that the only practical line to take at present was to permit the Egyptian sunna, which was acceptable to the Sudanese. Though a slightly more serious mutilation than that recognised by the 1946 legislation, which was unacceptable to them, it was at least 75% less damaging than the form now practised, and it had the great advantage that it did not interfere with childbirth. As one who had served for many years in the Sudan Sir Basil regretted that he had been forced to raise the subject in this public way. But the Sudanese were making rapid strides towards self-government, and they must realise that now they stood before the bar of public opinion. The practice would only come to an end when the Sudanese men themselves say that they will have nothing to do with women as brides who have been grossly mutilated in their early life.

In reply Mr. HECTOR MCNEIL, the Minister of State, pointed out that we were dealing with something which was not instinctive, but which was traditional, superstitious, and near religious, and which was certainly associated with sexual ignorance. The Sudanese service had to face the difficulties, the prejudices, and the deep feelings aroused by this subject. The 1946 legislation, for instance, had provoked a riot in the Blue Nile province. One woman doctor had already been appointed by the Sudan government and others were being appointed. But it would be a handicap to these women in their job if it was suggested that the primary reason for their appointment was to continue this kind of education. It must, he was sure, be related to the text of general progress. It was difficult, he continued, to get accurate figures, but he was assured that the pharaonic system of circumcision had decreased by 75% in the Khartoum area during the last 20 years. In the long run they must rely on the Sudanese themselves to excise this practice, but the Government would continue to watch the situation carefully, and would be grateful for any suggestion which might be passed on to the Sudan government.

1. See *Lancet*, 1946, i, 696.

QUESTION TIME

Care of the Old in Scotland

Mr. JAMES CARMICHAEL asked the Secretary of State for Scotland if he was aware that under the Scottish Poor Law Acts local authorities were obliged to provide hospital care for aged people, but since the repeal of these Acts this service was being neglected and in consequence great suffering was caused to old people living alone and in need of attention, particularly where there were no relatives; and if he would give this matter his attention and issue the necessary instructions to those possessing this authority to exercise it in the interest of the aged infirm.—Mr. ARTHUR WOODBURN replied: The facilities available for the hospital care of aged people have not decreased, but an increasing demand has caused some delay in the admission of old people not in urgent need of active medical treatment. The regional hospital boards are reviewing the situation to see what additional facilities can be made available.

Mr. CARMICHAEL: When the Minister indicates that the facilities are still there, may I ask him what body is responsible for doing this job, because we have been trying to find out in Glasgow and cannot do so? Is he aware that there are hundreds of aged people in Glasgow with nobody to care for them at all, and that this is a shocking state of affairs under a National Health Service?—Mr. WOODBURN: The facilities are no less now than before the service came into operation, but the regional boards are doing their best to increase them. I understand that the trouble has arisen, because a large number of old people, who were very much in need, would not seek this refuge because of the stigma which attached to the poor-law, but that they are now willing to take advantage of it because of the dignity attaching to the National Health Service.—Mr. CARMICHAEL: May I ask the Minister, where does he get the idea that there has been a change in the attitude of mind? Is he not aware that, for a good number of years, these aged people were cared for in hospitals, not workhouses, and that now there is evidence abroad that many of our voluntary hospitals are deliberately avoiding taking these people, who are being neglected by the community as a whole?

Colonel M. STODDART-SCOTT: Is not the Minister aware that there are fewer hospital beds for these people available now than on July 5?—Mr. WOODBURN: I am not aware of that. I do not think anybody has destroyed hospital beds.

Doctors' Withdrawals from N.H.S.

Sir HUGH LUCAS-TOOTH asked the Minister of Health how many general medical practitioners who had signified their willingness to enter the National Health Service had since gone out of the service; and whether he had any information to show what proportions of such practitioners had ceased to practise altogether, were now carrying on private practices, or had gone overseas with a view to practising abroad, respectively.—Mr. ANEURIN BEVAN replied: From July 5 up to Jan. 30, 497 general practitioners on the medical list had withdrawn, in addition 103 practitioners had died. In the same period 602 practitioners had joined the list. I have no information as to the reasons for the withdrawals.

Conditions of Service of Hospital Staffs

Dr. BARNETT STROSS asked the Minister when he would be able to submit his proposals on the terms and conditions of service of hospital staffs; whether he was aware that the delay is causing real hardship to ex-Service full-time consultants, whose remuneration is well below that of many other consultants who are employed part-time on a sessional basis; and whether, whilst discussions are taking place, he would consider making a retrospective payment of an interim nature.—Mr. BEVAN: I cannot say when the proposals will be available for publication, but I am doing all I can to complete discussions with the profession's representatives. Meanwhile I cannot contemplate any additional retrospective payment.

Central Health Services Council

Replying to a question, Mr. BEVAN stated that Mr. C. F. Comer had been lately appointed to the council. The council had met three times.

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Doctors of Institutions

Sir ROBERT YOUNG asked the Minister when information was likely to be given to those concerned regarding payment of basic salary for those undertaking general medical services for the staffs of institutions, seeing they were free from the liability of having persons assigned to them.—Mr. BEVAN replied: The adjustment of remuneration of practitioners with limited lists is among the matters to be dealt with in the distribution scheme which I am about to discuss with the profession.

Medical Partnerships

Mr. GEORGE JEGER asked the Minister when he intended introducing legislation to implement the findings of the Slade Committee on medical partnerships.—Mr. BEVAN replied: Legislation will be introduced this session.

Population

Replying to a question Mr. BEVAN stated that the civilian populations, including merchant seamen, at Dec. 31, 1948, were estimated as: England, 40,386,800; Wales, 2,552,200; Scotland, 5,120,200.

Family Allowances

In answer to a question Mr. JAMES GRIFFITHS, Minister of National Insurance, stated that the total amount paid in family allowances in the calendar year 1948 was approximately £58,750,000.

Unemployed Doctors

Sir WILLIAM DARLING asked the Minister of Labour how many registered medical practitioners were now reported as unemployed in Scotland and in England and Wales; for how long they had been unemployed; and what steps were being taken to utilise their services.—Mr. GEORGE ISAACS replied: The number of unemployed registered medical practitioners registered for employment at appointments offices on Feb. 14 was 18 in Scotland and 42 in England and Wales. Of these, 37 had been registered as unemployed for less than six months, 1 for eleven months, and 22—including 12 Poles—for over twelve months. In common with other registrants at appointments offices these men and women are submitted for any suitable vacancies notified to my Department.

Incidence of Venereal Disease in B.A.O.R.

Replying to a question, Mr. EMANUEL SHINWELL, Secretary of State for War, stated that the number of male officers and other ranks in B.A.O.R. who received treatment for venereal disease during 1948 represented approximately 8·8 per 100 strength.

Another Medical M.P.

Dr. A. D. D. Broughton, was returned as a Labour member in the recent by-election in the Batley and Morley division.

Press Portrait Bureau

Dr. Broughton, who is 46 years of age, is a native of Batley. He was educated at the grammar school there, at Rossall School, and the University of Cambridge. He qualified from the London Hospital in 1929. After holding house-appointments at Poplar Hospital and the London Hospital he became medical officer at Rossall School. In 1932 he settled in general practice at Batley where he is on the staff of the local hospital and a divisional surgeon of the St. John Ambulance Brigade. In 1936 he obtained the D.P.M. at Leeds, and the following year he took his M.A. and M.B. at Cambridge and the D.P.H. During the late war he served for five years with the R.A.F.V.R. with the rank of squadron-leader, acting as senior medical officer on various units in Bomber and Flying Training commands. In 1946 he was elected a town councillor of Batley.

Obituary

FRANCIS JAMES HENDERSON COUTTS

C.B., M.D., B.SC. MANC.

Dr. Coutts, a former senior medical officer of the Ministry of Health, died at Bournemouth on Feb. 13, at the age of 83.

He was born in Queensland, but his father, Robert Coutts, came from Windermere, and he returned to this country to study at Owens College and the University of Manchester, where he took his M.B. with honours in 1892. He held house-appointments at Manchester hospitals and a research fellowship in pharmacology at Owens College before he was appointed assistant to Sheridan Delépine, who then held the Manchester chair of pathology. In 1898 he was awarded the gold medal for his M.D. thesis. In 1899 Coutts joined the staff of the public-health department of the university, and two years later he became medical officer of health for Blackpool. To fit himself for his new specialty he took the D.P.H. in 1900 and seven years later he obtained his B.SC. in public health. When in 1908 he entered the central health department as a medical inspector of the Local Government Board he already had a high reputation as a research-worker in pharmacology and a competent and successful M.O.H. His first work at the board was in the foods branch, where he used his wide knowledge of chemistry in investigations on condensed and dried milks and proprietary foods in relation to their value in infant feeding.

When the national tuberculosis service was set up in 1912, Sir Arthur Newsholme entrusted Coutts with the direction and planning of its medical administration. In him he found a conscientious and indefatigable worker and an ideal coadjutor, and in 1915 he entrusted him with the new venereal-diseases scheme. Coutts's administrative success in this field was recognised by his election as president of the Society for the Study of Venereal Diseases. In 1919, when the Ministry of Health was founded, he became senior medical officer of the tuberculosis and venereal-diseases branch of the medical department, a post which he held till his retirement in 1930.

In his busy life he made time for other activities. He examined in public health for Liverpool, Manchester, Birmingham, and Leeds universities. As a Freemason he attained to high rank in the craft. He enjoyed gardening, was an enthusiastic motorist, played golf, and was a member of the Savage Club.

Coutts's duties at the Ministry had brought him into close association with the work of the Welsh National Memorial Association. Professor Lyle Cummins writes: "The Adelina Patti Hospital, the hospital at Cefn Mably, and the first stirrings of the idea of the great hospital at Sully, were all matters on which his advice and help were often wanted and always available, and it was a great advantage to me to feel that I had behind me such an eminent adviser and valuable ally." In 1938 this side of his work was rounded off when Sir Kingsley Wood, the Minister of Health, appointed a committee consisting of Mr. Clement Davies, M.P., and Dr. Coutts, to inquire into the anti-tuberculosis service in Wales and Monmouthshire. Their report, published in 1939, did much good through stimulating coördination of the work of local authorities in Wales with that of the Welsh National Memorial Association.

Sir Arthur MacNalty, to whom we owe much of this memoir and who succeeded Coutts in his post at the Ministry, writes: "In all his work I was for many years closely associated with Coutts. He proved himself a kind and considerate chief whose integrity and justice inspired loyalty and confidence in his staff. Up to last year his letters to me showed that he retained his interest in medical and public-health affairs, but towards the end of the year his health failed. I mourn the loss of a friend and cherish the memory of his able and comprehensive work, which has done much to combat two deadly diseases of mankind."

Coutts was appointed C.B. in 1923. He married in 1899 Miss Elizabeth Boullen of Ambleside and they had two daughters.

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Notes and News

THE SENIOR CIVIL SERVANT'S PAY

THE committee appointed, under the chairmanship of Lord Chorley, to advise on remuneration in the higher grades of the Civil Service, has recommended [1] improvements which will amount to a total of about £200,000–400,000 per annum and will be gradually introduced. Three good reasons are put forward in support of this change: (1) that the work is becoming increasingly complex and responsible, and that even in 1939 substantial increase of salaries for the highest posts was already overdue; (2) that a number of Government-sponsored employments (for example, specialists in the National Health Service and the staffs of nationalised industries) now offer rewards greatly in advance of those in the Civil Service; and (3) that the cost of living is now much heavier.

> "... the improvements upon 1939 salary which have been granted to the highest Civil Service grades (e.g., Permanent Secretary 17 per cent., Deputy Secretary 14 per cent.) are a good deal smaller than those which have been granted, speaking generally, in other employments and in the lower grades of the Civil Service itself."

The proposed increments for the administrative group range from £1250 in the case of the permanent secretary to the Treasury (bringing his salary to £5000) to £300 for an assistant secretary, bringing his maximum to £2000. Remuneration of other groups should be adjusted accordingly. The committee are on the whole satisfied with the "salary relativities" between the administrative class and the professional and technical classes; but they are more dubious about the "career relativities." While it should be exceptional for a professional or technical Civil Servant to be paid more than the permanent secretary of his department, there is no reason why this should not happen now and then when men of professional or technical eminence are appointed for duties outside the ordinary team-work of the department. A scientific Civil Service is being gradually founded; and a similar development should be encouraged in the other professional and technical classes.

In the Civil Service "dazzling individual awards are inappropriate," and salaries in the higher grades should not be determined on a purely competitive basis; yet senior Civil Servants should not have to adopt a considerably lower standard of living than people of comparable status in other employments. It has long been obvious that the salaries offered to medical men and women in the Civil Service should be brought into closer relation with those obtainable by their colleagues outside.

THE ROARING VOICE FROM EDINBURGH

PLAYS dealing with the real deeds of real people are uncommonly tricky to write, and usually (unless signed W. Shakespeare) uncommonly vexing to watch. Truth will out, if not from the author's ink-well, then from the expostulating memory of the watcher; and, like a bad wife amending her husband's anecdote, she strikes the performance dead. *The Human Touch*, by J. Lee-Thompson and Dudley Leslie, now running at the Savoy Theatre, and dealing with Sir James Simpson's discovery of chloroform, ought by rights to suffer this fate in the first ten minutes; oddly enough, it doesn't. It matters little that young Dr. Simpson did not discover the use of chloroform until eight years after the play finishes, or that he was the father of a large family (the solitary sickly boy of the play was not born till three years later, and did not die until his father was fifty), or that Simpson's colleagues never sat round his table attempting to certify him as insane; these are merely examples of the shifts to which playwrights are driven when trying to present a lifetime dramatically. A more serious liberty is taken with Dr. Simpson's character: very little is left of that audacious merry fighter, who took such keen delight in putting down opponents with a counterblast of evidence and mockery. This Simpson shares with his original a passionate dislike of pain, but is otherwise a stranger to him: the vigour, the fun, and the essential toughness are missing. The authors present instead a young, sensitive, and troubled Simpson, opposed by colleagues whose professional manners take a deal of swallowing—by the audience no less than the victim. It is the play's triumph that they *can* be swallowed along with all the other camels, because the writing is sincere, and sets out well and even movingly Simpson's case against the waste of life and spirit caused by pain. There are plenty of other holes to be picked in the piece; but it is about something real, about a controversy not yet dead, and as such is better worth seeing than many other plays now running in London. And it is superbly acted.

1. Report of the Committee on Higher Civil Service Remuneration. Cmd. 7635. H.M. Stationery Office. Pp. 14. 4*d*.

CALL-UP OF DOCTORS TO THE FORCES

UNDER a new ruling announced by the Central Medical War Committee doctors called up to the Forces from Jan. 1 this year are required to serve for 18 months. The upper age-limit for those engaged as either specialist or general-duty officers is 30 years, with the exception of the doctor who makes a successful application to the Ministry of Labour, through the Central Medical War Committee, for postponement of call-up on grounds of exceptional personal hardship; such a doctor is then still liable for recruitment beyond his 30th birthday for the length of the period during which the postponement certificate is in force.

These arrangements differ somewhat from those in 1948. Then, the upper age-limit for the call-up of specialists was 35 years; doctors over 26 years of age were exempted from call-up as general-duty officers unless they had been granted deferment to enable them to obtain further qualifications or special experience, in which case they were subject to recruitment up to their 30th birthday.

TOWARDS BETTER MENTAL CARE IN AMERICA

THE lack of trained psychiatrists is as acute in America as here. The American Psychiatric Association puts the number practising in the whole of the United States as less than 5000, and nearly 1000 appointments are unfilled. The need is particularly urgent in the State mental hospitals, community clinics, and Veterans Administration hospitals. The U.S. Public Health Service estimates the total need for psychiatrists at 15,000. Dr. William C. Menninger, president of the association, recently announced that an institute—or, as we would say, a postgraduate course—will be held in Philadelphia from April 11 to 15, under the association's auspices. It is open to staffs of public and private hospitals, and to doctors and laymen in the United States and Canada. The programme of instruction will be under the direction of Dr. Daniel Blain, medical director of the association, and will cover current problems of administrative procedure, staff shortages, overcrowding, financial support, and related problems. The institute is being held at a time when the public have become seriously concerned over conditions in State mental hospitals, and when the governors of Minnesota, Massachusetts, Maryland, New York, and other States are taking part in a drive to bring standards up to the level advocated by the association.

University of Oxford

Mrs. Antoinette Pirie has been appointed Margaret Ogilvie reader in ophthalmology with effect from April 1.

University of London

On Thursdays, March 3 and 10, at 5 P.M., at St. Thomas's Hospital medical school, Albert Embankment, London, S.E.1, Mr. A. Ll. Hodgkin, F.R.S., will lecture on Ionic Exchange and Electrical Activity in Nerve and Muscle.

University of Leeds

Dr. Wallace Ironside has been appointed senior lecturer in psychiatry.

University of Sheffield

Dr. Q. H. Gibson has been appointed senior lecturer in physiology, Dr. R. Gordon honorary lecturer in child health, and Dr. H. R. Worth assistant medical officer to the student health service of the university and to the nursing-staff health service of the United Sheffield Hospitals.

Leeds Regional Hospital Board

The scheme for the development of a diagnostic treatment and research centre at Harrogate submitted to the Minister of Health by the board is a long-term project. The Minister has approved the first stage, which is the purchase by the board of the White Hart Hotel for £27,500. This accommodation is to be used for ambulant patients not needing complete or highly specialised nursing care and attention.

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Bristol Medical Re-union

A dinner will be held on April 30 in Bristol. For particulars apply to Dr. Richard Clarke, Harley Lodge, Clifton Down, Clifton, Bristol, 8.

Department of Scientific and Industrial Research

Sir Edward Appleton, F.R.S., who was lately appointed principal of Edinburgh University, is to be succeeded as secretary of the Department by Sir Ben Lockspeiser, chief scientist to the Ministry of Supply.

W.H.O. Eastern Mediterranean Conference

At the conclusion of this conference, on Feb. 11, Sir Aly Tewfik Shousha, Pasha, Egyptian under-secretary of state for health, and chairman of the W.H.O. executive board, was unanimously nominated director of the Eastern Mediterranean regional office, to be established at Alexandria.

Medical Illustrators

A meeting will be held for medical and surgical artists at the Radcliffe Infirmary, Oxford, on Saturday, April 2, at noon, to form an association of medical illustrators. Further information may be had from Mrs. Zita Stead Blackburn, provisional hon. secretary, 19, York Avenue, East Sheen, London, S.W.14.

Rations and Allowances for Diabetics

The Ministry of Food, in response to queries raised about the rations and allowances available to patients with diabetes mellitus, states that instead of their sugar ration and the ordinary allowance of cheese they should receive 2 extra rations of meat a week, 12 oz. of cheese a week, 12 oz. extra butter/margarine. They may also have 7 pints a week of milk if prescribed.

Nuffield Fellowships

The Nuffield Foundation have widened the scope of their medical fellowships, which are now offered in all fields of medicine, though special consideration will still be given to child health, industrial health, social medicine, and psychiatry. Fellowships are also being offered to medical men and women holding higher qualifications, to enable them to be trained in the diagnosis, treatment, and study of chronic rheumatism. Further information will be found in our advertisement columns.

British Tuberculosis Association

The annual conference of the association will be held at Trinity College, Cambridge, from April 6 to 9. The speakers will include: Dr. J. B. McDougall, W.H.O. and Tuberculosis; Dr. R. H. Hazemann (Paris), Tuberculosis in Students and Teachers in France; Mr. Irving Sarot (New York), Resection for Pulmonary Tuberculosis; Mr. S. J. McHale, Post-operative Course of Thoracoplasty Cases; Dr. J. A. Young, Vaccination of Cattle with the Vole Bacillus; Dr. W. E. Ogden (Toronto), Preclusion of Tuberculous Disease by Preclinical Diagnosis and Control; Dr. J. M. Lemoine (Paris) and Dr. Conrad Xalabarder (Barcelona), Atelectasis; Mr. John Francis, M.R.C.V.S., Infection with the Bovine Tubercle Bacillus; Miss Honor Fell, D.SC., Relationship between Cells and Tubercle Bacilli in Tissue Culture and in Vivo; Dr. E. M. Brieger and Dr. B. R. Smith, Life History of Tubercle Bacilli.

Medical Research Council

The council have appointed the following committee to advise and assist them in the prosecution of research on the carcinogenic action of mineral oils:

T. FERGUSON, M.D., professor of public health, University of Glasgow (chairman).
Colonel S. J. M. AULD, D.SC., chairman of research group no. 2, Institute of Petroleum.
J. W. COOK, D.SC., F.R.S., professor of chemistry, University of Glasgow.
ALEXANDER HADDOW, M.D., D.SC., professor of experimental pathology, University of London, at the Royal Cancer Hospital.
J. O. IRWIN, D.SC., senior research-worker, M.R.C. statistical research unit, London School of Hygiene.
J. R. SQUIRE, M.D., professor of experimental pathology, University of Birmingham.
D. L. WOODHOUSE, PH.D., officer in charge, cancer research laboratory, University of Birmingham.
J. M. ROGAN, M.D., M.R.C. headquarters staff (secretary).

The Ministry of Fuel and Power, the Ministry of Health, and the Ministry of Labour have nominated representatives to attend meetings.

International Congress on Rheumatic Diseases

More than 150 doctors from other countries are expected to attend this congress in New York from May 30 to June 3. The speakers will include: Lord Horder, Dr. Jacques Forestier (Aix-les-Bains), Dr. Eric Jonsson (Stockholm), Prof. S. de Sèze (Paris), and Dr. William Tegner. Further information may be had from Dr. E. P. Jordan, 2020, East 93rd Street, Cleveland 6, Ohio.

S.-E. Metropolitan Regional Tuberculosis Society

At a meeting of this society held at Preston Hall, on Jan. 22, with Dr. F. Temple Clive in the chair, the constitution of the society was confirmed. On March 12, at 10.30 A.M., at Queen Mary's Hospital, Sidcup, Dr. F. R. G. Heaf will lecture on B.C.G. A clinical meeting will be held at the Royal Sea Bathing Hospital, Margate, on May 14.

Oliver Memorial Fund

The committee of this fund will make the second award of the value of £50 to a British subject whose original work or service in connexion with blood-transfusion is considered to be a notable contribution to the research, organisation, or donor aspect of this subject. Applications or communications drawing attention to suitable candidates should be sent before June 30 to the hon. treasurer, Mr. F. W. Mills, National Provincial Bank Ltd., Holborn Circus, London, E.C.1.

Royal Institute of Public Health and Hygiene

The lectures to be given at the institute, 28, Portland Place, London, W.1, during March and April include: Mr. L. Z. Cosin, Social Significance of Geriatric Rehabilitation (March 23); Dr. L. G. Housden, Growing Family under Modern Home Conditions (April 6); Mr. Joseph Minton, Occupational Eye Diseases and Injuries (April 20 and 27). The lectures will be held at 3.30 P.M.

Royal Society

Prof. H. Raistrick, F.R.S., will give the Bakerian lecture for 1949 on May 12.

The Croonian lecture for 1949 will be delivered on June 30 by Dr. D. W. Bronk, FOR.MEM.R.S.

Dr. Bronk is foreign secretary of the National Academy of Sciences, chairman of the National Research Council of the U.S.A., and director of the Johnson Institute for Medical Physics in the University of Pennsylvania. His special field of work has been the physiology of the nervous system and his recent work has been on the oxygen consumption of the brain.

Tata Memorial Trust

The trustees of the Lady Tata Memorial Fund invite applications for grants and scholarships for research in diseases of the blood, with special reference to leukæmia, in the academic year beginning on Oct. 1.

Grants of variable amount are made for research expenses or to provide scientific assistants for senior workers. Scholarships are awarded as personal remuneration; their normal value has been £400 per annum for whole-time research, with proportionate adjustment for work on a part-time basis, where this has been approved. Applications must be submitted before March 31. Further particulars may be had from the secretary of the scientific advisory committee, c/o Medical Research Council, 38, Old Queen Street, London, S.W.1.

W.H.O. Research on Tuberculosis

In the mass immunisation campaign against tuberculosis now being carried out jointly by the Danish Red Cross and its Scandinavian affiliates, with the coöperation of UNICEF and the World Health Organisation, about 8 million children in Europe have been tested and 3 million immunised with B.C.G. The cards made out for every person tested, and other pertinent information relating to the campaign, will be analysed in Copenhagen by a staff directed by Dr. Carroll Palmer, who has been released from the United States Public Health Service for this purpose. They will serve as a basis for research projects, including investigation of criteria for B.C.G. vaccination, revaccination, the statistical aspects of the campaign, research on the effectiveness of B.C.G., and the level of tuberculin sensitivity of children. Basic studies on tuberculosis also will be undertaken, among them research into racial and familial susceptibility and resistance to tuberculosis and response to artificial immunisation. It is expected that the fungus infection, histoplasmosis, which in many ways resembles tuberculosis, will also be studied. Dr. Palmer is taking up his work at once and will be joined by Dr. Lydia Edwards, of the U.S. Public Health Service, and Dr. I. C. Yuan, former deputy minister of health in China, who will act as his deputy.

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International Society of Medical Hydrology

The annual meeting of this society will be held from Oct. 9 to 15, in Dax (Landes) France. Further particulars may be had from the hon. secretary, Dr. Donald Wilson, Cranbourne, Southdown Road, Bognor Regis, Sussex.

Association of Sea and Air Port Health Authorities

The annual meeting of this association will be held at the Town Hall, Newport, Mon., on April 27–29. Dr. Stuart Laidlaw will read a paper on Imported Fats, Sir Harold Whittingham on the Control of Water and Food Supplies on Air Routes, Dr. L. H. Murray on Experiences of an Army Hygiene Officer, and Dr. T. L. J. Coxon on Port Health and its Relation to Allied Services. Further information may be had from the hon. secretary, Dr. H. C. Maurice Williams, health department, Civic Centre, Southampton.

Railway Executive Appointment

Dr. H. H. Cavendish Fuller has been appointed chief medical officer to the Railway Executive.

Dr. Fuller was educated at Bishops Stortford and Edinburgh University. After medical work at home and in the East, he joined the R.A.M.C. in 1914, and served as a medical officer with the Royal West Kent Regiment at home and overseas. Later he was in charge of Princess Marie Louise Hospital, Bermondsey. In civilian life he was in general practice, and was medical officer to Malvern College from 1917 to 1930. He was appointed assistant chief medical officer to the G.W.R. in 1930, and chief medical officer in 1931. During the late war Dr. Fuller held the rank of lieut.-colonel in the Home Guard. In March, 1948, he was appointed medical adviser to the Railway Executive.

Prof. S. Zuckerman, F.R.S., a member of the Advisory Council on Scientific Policy and of the Committee on Industrial Productivity, has been appointed deputy chairman of both bodies. Dr. Zuckerman will continue to hold the chair of anatomy at Birmingham University.

Dr. K. J. Powell, anæsthetist to Sheffield City General Hospital, is to give a three-month course on anæsthesia at the Institute of Pathological Surgery in Rome and to lecture for the British Council in Florence and Milan.

The M.R.C. memorandum (no. 19) on the Rh Blood Groups and their Clinical Effects (*Lancet*, 1948, ii, 502) has been revised and reprinted. It is obtainable, price 1*s.* 6*d.*, from H.M. Stationery Office.

The report of the third national conference on the Care of Old People arranged by the National Old People's Welfare Committee (National Council of Social Service, 25, Bedford Square, London, W.C.1. 1948. Pp. 43. 2*s.*) gives the views of many of the 700 delegates who attended. The report includes Dr. Trevor Howell's address on the Care of the Aged Sick, and Dr. T. Ruddock-West's paper on Coöperation between Statutory and Voluntary Bodies under Existing Legislation.

CORRIGENDUM.—*Estimation of Basal Metabolic Rate.* In Dr. Robertson's letter of Feb. 19 (p. 324), line 14 should read: "... may be none of these."

Appointments

ALWYN-SMITH, PETER, M.B. Lond.: M.O. on headquarters staff, Welsh Regional Hospital Board.
BARNES, E. G., M.B. Edin.: asst. tuberculosis M.O. to North-Eastern Regional Hospital Board, Scotland.
CRUICKSHANK, M. M., C.I.E., M.D. Aberd., F.R.C.S.E., F.A.C.S., D.O.M.S.: senior asst. medical superintendent, Aberdeen General Hospitals.
GORDON, R. R., M.C., M.D. Glasg., M.R.C.P., D.OBST.R.C.O.G., D.C.H.: pædiatrician, City General Hospital, Sheffield.
GUILD, A. B., M.B. Edin., D,T.M. & H., D.P.H.: asst. county M.O. and M.O.H., local health area no. 3, Norfolk.
HAMILTON, A. D. M., M.B. Belf., D.P.H.: asst. chest physician, Southampton area.
HILDITCH, J. H., M.B. Manc., D.P.H.: M.O.H., Wigan.
HITCHENS, R. A. N., M.B. Wales, D.P.H.: M.O. for student welfare, University of Wales.
JONES, W. L., M.B. Durh., D.P.M.: senior consultant physician, Mapperley Hospital.
RAFFAN, J. B., M.B. Aberd.: pathologist, Mid and West Glamorgan group of hospitals.
READ, A. M., M.B.: asst. chest physician, Chichester area.
ROBERTS, R. A., M.B., B.SC. Lpool, D.M.R.E.: radiologist, Mid and West Glamorgan group of hospitals.

Colonial Service:

EATON, R. D. P., M.B. Manc.: M.O., Sierra Leone.
LOCKYER, J. C. G., M.A., B.M. Oxfd: M.O., Tanganyika.
ROBINSON, EDWARD, M.B. Sheff.: M.O., Nyasaland.

Diary of the Week

FEB. 27 TO MARCH 5

Monday, 28th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Dr. R. A. Russell Taylor: Ætiology, Pathology, Diagnosis and Treatment of Acute Pancreatitis. (Hunterian lecture.)
UNIVERSITY COLLEGE, Gower Street, W.C.1
4.45 P.M. Prof. C. Rimington, D.SC.: Haem Pigments in Nature. (First of two lectures.)
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
9 P.M. Dr. Horace Evans: Richard Bright—Before and After. (First Lettsomian lecture.)
HUNTERIAN SOCIETY
8.30 P.M. (The Mansion House, E.C.) Sir Heneage Ogilvie: Personal Experiences. (Hunterian oration.)

Thursday, 3rd

UNIVERSITY OF LONDON
5 P.M. (St. Thomas's Hospital Medical School, S.E.1.) Mr. A. Ll. Hodgkin, F.R.S.: Ionic Exchange and Electrical Activity in Nerve and Muscle. (First of two lectures.)
INSTITUTE OF PSYCHIATRY
4.30 P.M. (Maudsley Hospital, S.E.5.) Mr. Terence Cawthorne: Physiology of the Vestibular Apparatus.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, S.W.1
4.30 P.M. Psychiatry lecture-demonstration.
SOCIETY FOR THE STUDY OF ADDICTION
5 P.M. (1, Wimpole Street, W.1.) Dr. Pablo Wolff: Problems of Drug Addiction in South America. (Kelynack lecture.)
ROYAL PHOTOGRAPHIC SOCIETY, 16, Prince's Gate, S.W.7
7 P.M. *Medical Group.* Dr. J. M. Tanner, Dr. Brian Stanford: Somatotyping—Purpose and Method.

Friday, 4th

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. Bertram Jones: Atypical Pneumonia.

Saturday, 5th

NUTRITION SOCIETY
10.30 A.M. (London School of Hygiene, Keppel Street, W.C.1.) Dr. H. E. Magee (chairman), Mr. John Hammond, F.R.S., Mr. A. Walton, Mr. S. Folley, D.SC., Prof. A. St. G. Huggett: Nutrition and Fertility.

Births, Marriages, and Deaths

BIRTHS

ALEXANDER.—On Feb. 14, at Cheltenham, the wife of Mr. A. F. Alexander, F.R.C.S.E.—a daughter.
ALEXANDER.—On Feb. 16, in London, the wife of Dr. A. B. Alexander—a son.
BAILY.—On Feb. 16, at Bristol, the wife of Dr. R. A. J. Baily—a son.
BLAINEY.—On Feb. 7, at Cambridge, the wife of Dr. J. D. Blainey—a daughter.
FOSTER-SMITH.—On Feb. 14, in London, the wife of Dr. G. C. Foster-Smith—a daughter.
GOOLDEN.—On Feb. 12, the wife of Dr. A. W. G. Goolden—a son.
GRAHAME.—On Feb. 11, at Boreham Street, Sussex, the wife of Dr. Colin Grahame—a son.
HOLLAND.—On Feb. 16, at Epsom, the wife of Dr. H. W. Holland—a daughter.
HOUSTON.—On Feb. 12, in London, the wife of Dr. J. C. Houston—a son.
LEVI.—On Feb. 11, at Liverpool, to Dr. Pearl Levi (née Lyons), wife of Dr. H. T. Levi—a son.
LEVINSON.—On Feb. 12, in London, to Dr. Frances Levinson (née Dove), wife of Mr. Ellis Levinson—a son.
NEILL.—On Feb. 14, at Bath, the wife of Dr. Gordon Neill—a daughter.
PINKERTON.—On Feb. 16, at Cambridge, the wife of Dr. J. R. H. Pinkerton—a son.
ROTH.—On Jan. 20, at Dumfries, the wife of Dr. Martin Roth—a daughter.
SEAVER.—On Feb. 8, at Leicester, the wife of Dr. R. G. Seaver—a son.
WASS.—On Feb. 11, in London, the wife of Mr. S. H. Wass, F.R.C.S.—a son.

MARRIAGES

KILPATRICK—STAUNTON.—On Feb. 9, in London, Kenneth Kilpatrick, B.M., to Mary Staunton, M.B.

DEATHS

BROCK.—On Feb. 16, at Westwell, Kent, George Sandison Brock, M.B.E., M.D. Edin., M.D. Rome, F.R.C.P.E., F.R.S.E., aged 90.
CHADBORN.—On Feb. 18, at Burgess Hill, Charles Nugent Chadborn, M.R.C.S.
COUTTS.—On Feb. 13, at Bournemouth, Francis James Henderson Coutts, C.B., M.D. Manc., D.P.H., aged 83.
ENSOR.—On Feb. 10, Cecil Arthur Ensor, M.R.C.S., aged 75.
FRIEDLAENDER.—On Feb. 20, Kate Friedlaender, M.D. Innsbruck, M.D. Berlin., D.P.M.
GARDE.—On Feb. 17, at Falmouth, Walter Henry Ormonde Garde, F.R.C.S.E., surgeon captain, R.N. retd, aged 78.
HOLMES.—On Feb. 11, at Eastbourne, Bernard Willoughby Holmes, M.R.C.S.
SOMERVILLE.—On Feb. 19, Edgar Somerville, M.D. Edin., F.R.C.S.E., aged 74.
THOMS.—On Feb. 11, in London, Geoffrey Surridge Thoms, M.B. Edin., surgeon commander, R.N.

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